The opinion in support of the decision being entered today is not binding precedent of the Board.

Paper ~~108~~ 11

By: Trial Section Merits Panel
Board of Patent Appeals and Interferences
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
Tel: 703-308-9797
Fax: 703-305-0942

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

ALFRED C. NICHOLS and K. LEMONE YIELDING

Junior Party
(Patent 5,783,700)

v.

BORIS TABAKOFF, LAWRENCE SNELL
and PAULA L. HOFFMAN

Senior Party
(Application 09/171,697)

Patent Interference No. 104,522

Before: SCHAFER, SPIEGEL and TIERNEY, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

FINAL JUDGMENT

I. Summary

This interference is between Patent 5,783,700 issued to Alfred C. Nichols and K. Lemone Yielding (**Nichols**) and Application 09/171,697 of Boris Tabakoff, Lawrence

Snell and Paula L. Hoffman (**Tabakoff**). The involved subject matter relates to 4-urea (i.e., 4-ureido) derivatives of kynurenic acid, a class of antagonists of N-methyl-D-aspartate (NMDA) receptors in the brain, useful for treating conditions involving overstimulation of NMDA receptors, e.g., alcohol or drug withdrawal symptoms or epilepsy (Ex 2009, ccs. 1-2; Ex 2011, pp. 7-9).

There is no disagreement that Tabakoff asked Nichols to synthesize 4-urea derivatives of kynurenic acid ("4-urea derivatives") in order to study their efficacy in treating alcohol withdrawal symptoms or that Nichols performed synthetic activities as a result of Tabakoff's request. The disagreement is over the nature of the collaborative relationship between the two parties. Tabakoff contends that Nichols performed routine synthetic activities on its behalf, while Nichols argues that those activities rose to the level of inventorship because Tabakoff did not suggest any specific (i.e., disubstituted) 4-urea derivative or synthesis method therefor. Nichols further argues that after "extensive" experimentation it actually reduced the invention to practice before Tabakoff's effective filing date and provided Tabakoff with detailed information regarding the design and synthesis of the 4-urea derivatives. Nichols still further argues that Tabakoff's failure to list Nichols as joint inventors of Tabakoff's claims amounts to inequitable conduct before the U.S. Patent and Trademark Office (PTO). According to Tabakoff, Nichols' patent violates the best mode requirement by failing to disclose fully details of Nichols' synthesis method (e.g., order of addition of reagents, stoichiometry of the reaction, and isolation and purification of the claimed compounds).

We award judgment against Nichols. Nichols' evidence is insufficient to prove (1) that Nichols actually reduced the invention to practice before Tabakoff's effective filing date, (2) that Tabakoff derived the invention from Nichols, (3) that Nichols is a joint inventor of Tabakoff's involved claims, or (4) that Tabakoff acted inequitably before the PTO. Since priority is not awarded to Nichols, the issue of whether the Nichols patent violated the best mode requirement of 35 U.S.C. § 112, ¶ 1 is moot.

II. Background

1. Nichols is involved in this interference on the basis of U.S. Patent 5,783,700 ("Nichols '700," Ex 2009), granted July 21, 1998, based on application 08/887,627, filed July 3, 1997.

2. Nichols' real party-in-interest is the named inventors.

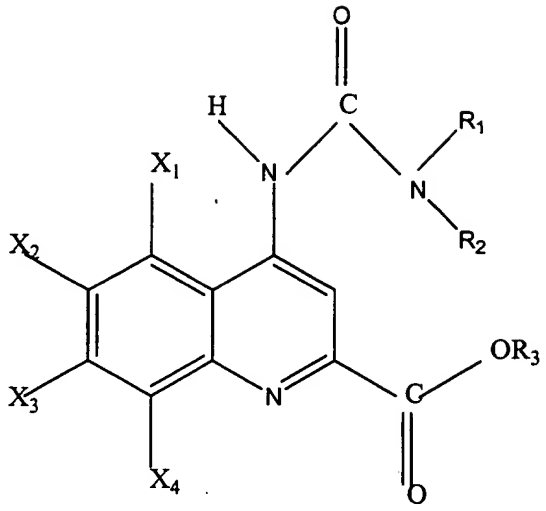
3. Tabakoff is involved in this interference on the basis of application 09/171,697, filed October 23, 1998 ("Tabakoff '697," Ex 2011). Tabakoff '697 has been accorded benefit for the purpose of priority of the June 6, 1997 filing date of its U.S. provisional application 60/048,848 (Ex 1006).

4. Tabakoff's real party-in-interest is LOHOCLA RESEARCH CORPORATION.

5. The subject matter of the interference is defined by one Count, i.e., a compound according to any of claims 1 or 15 of Nichols or a compound according to claim 12 of Tabakoff.

6. Nichols compound claim 1 reads:

A compound of the formula:



wherein

R_1 is selected from the group consisting of hydrogen, ethyl, methyl, n-butyl, or phenyl,

R_2 is selected from the group consisting of hydrogen, ethyl, methyl, n-butyl, phenyl, or 3-methoxyphenyl;

R_3 is selected from the group consisting of ethyl, methyl, or hydrogen;

X_1 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms;

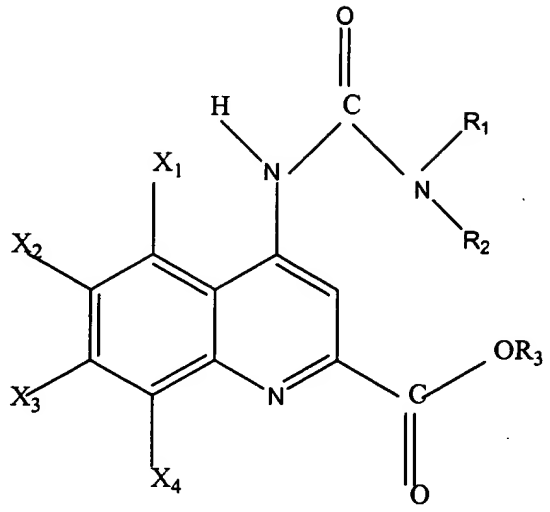
X_2 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms;

X_3 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms; and

X_4 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms.

7. Nichols compound claim 15 reads:

A compound of the formula:



wherein

R_1 is selected from the group consisting of hydrogen or any branched or straight-chained alkyl group containing from 1 to 6 carbon atoms;

R_2 is selected from the group consisting of hydrogen or any branched or straight-chained alkyl groups containing from 1 to 6 carbon atoms;

R_3 is selected from the group consisting of ethyl, methyl, or hydrogen;

X_1 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms;

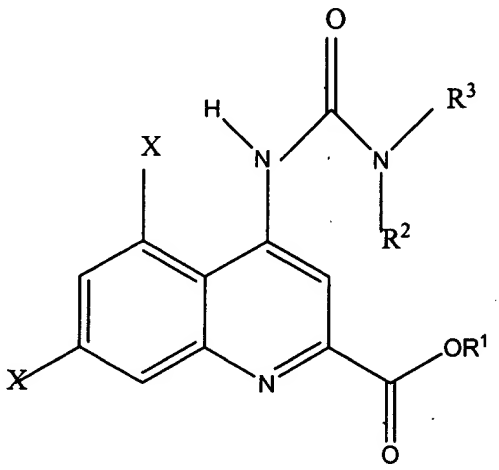
X_2 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms;

X_3 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms; and

X_4 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, iodo, nitro, cyano, fluoromethyl, any branched or straight-chained alkyl group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy group containing from 1 to 4 carbon atoms, any branched or straight-chained alkoxy carbonyl group containing from 1 to 4 carbon atoms, or any branched or straight-chained acyl group containing from 1 to 4 carbon atoms.

8. Tabakoff compound claim 12 reads:

A compound for treating withdrawal syndromes manifested in a patient suffering withdrawal symptoms and/or withdrawal-induced brain damage and having the formula (I):



a tautomer thereof, a pharmacologically acceptable ester, amide, salt, ether, or an acid addition salt thereof;

wherein R^1 represents hydrogen or an alkyl group of 1 to 3 carbon atoms;

R^2 and R^3 each independently represent phenyl which may be unsubstituted or alkoxy substituted one or more times with alkoxy containing 1 to 3 carbon atoms,

wherein each of the R^2 and R^3 substituents can be the same or different; and

X represents halogen and each of the 5,7 substituents can be the same or different.

9. All originally issued Nichols claims, i.e., claims 1-15, correspond to the Count (Paper 1, p. 47).

10. Of total pending Tabakoff claims 11-19 and 21-23, only claims 11-15, 18 and 19 correspond to the Count (Paper 1, p. 47).

11. After the interference was declared, preliminary motions were filed by both parties. As a result of the MEMORANDUM OPINION and ORDER (Paper 56),

(a) Nichols reissue application 09/625,018 (Ex 2010) with reissue claims 1-42 was added to the interference and Nichols reissue claims 1-28[1] were designated as corresponding to the Count (Paper 56, pp. 9-32, "Nichols preliminary motion 3");[2]

(b) Nichols preliminary motion 1, alleging that involved Tabakoff claims 11-15, 18 and 19 are unpatentable under 35 U.S.C. § 102(f) for incorrect inventorship, was deferred to final hearing (id., pp. 33-36);

(c) Nichols preliminary motion 3, alleging that Tabakoff acted inequitably by failing to inform the PTO of Nichols' inventorship claim, was deferred to final hearing (id., pp. 42-44); and,

(d) Tabakoff preliminary motion 1, alleging that Nichols claims 1-15 are unpatentable for failing to satisfy the best mode requirement of § 112, ¶ 1, was denied without prejudice, subject to renewal based on evidence acquired during the priority phase of the interference or other evidence developed as result of priority phase testimony (id., pp. 37-42).

12. Subsequently, a schedule was set for the priority phase of the interference. Only Nichols filed any evidence on priority. Tabakoff elected to rely on the June 6, 1997 filing date of its provisional application 60/048,848 as a constructive reduction to

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[1] Nichols reissue claims 1-15 are identical to originally issued claims 1-15.

[2] Nichols reissue claims 29-42 were designated as not corresponding to the Count; and, are unpatentable for failure to comply with the written description requirement of 35 U.S.C. § 112, ¶ 1. In addition, there is no interference-in-fact between Nichols reissue claims 29-42 and Tabakoff claims 16-17 (which the examiner has found to be patentable). [Paper 56, p. 32, n.3.]

practice (Paper 74).

III. Priority

"Priority goes to the first party to reduce an invention to practice unless the other party can show that it was the first to conceive the invention and that it exercised reasonable diligence in later reducing the invention to practice." Price v. Symsek, 988 F.2d 1187, 1190, 26 USPQ2d 1031, 1033, (Fed. Cir. 1993).

"A rebuttable presumption shall exist that, as to each count, the inventors made their invention in the chronological order of their effective filing dates. The burden of proof shall be upon a party who contends otherwise." 37 CFR § 1.657(a). Thus, in an interference involving "a patent and an application having an effective filing date on or before the date of patent issued, a junior party shall have the burden of establishing priority by a preponderance of the evidence." 37 CFR § 1.657(b).

Nichols argues that it "conceived of the invention corresponding to the interference count and reduced the invention to practice prior to the constructive filing date of the Senior Party"(NB, p. 41, ¶ 2).[3] Nichols does not argue that it was the first to conceive and the last to reduce the invention to practice or assert diligence from before Tabakoff's effective filing date to an actual or constructive reduction to practice. Nichols further argues that Tabakoff derived the subject matter of the interference from Nichols.

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[3] Herein, "NR" refers to Nichols Record, "NB" to Nichols Principal Brief (Paper 84), "TO" to Tabakoff Opposition to Nichols Principal Brief (Paper 90), and "NRB" to Nichols Reply Brief to Tabakoff Opposition to Nichols Principal Brief (Paper 94). Similarly, "TR" refers to Tabakoff Record, "TB" to Tabakoff Principal Brief (Paper 88), "NO" to Nichols Opposition to Tabakoff Principal Brief (Paper 96) and "TRB" to Tabakoff Reply Brief to Nichols Opposition to Tabakoff Principal Brief (Paper 97).

Thus, we turn to Nichols' priority and derivation cases.

A. Actual reduction to practice

In order to establish actual reduction to practice, the inventor must prove that he constructed an embodiment or performed a process that met all the limitations of the claim, and that he determined that the invention would work for its intended purpose. Slip Track Systems, Inc. v. Metal-Lite, Inc., 304 F.3d 1256, 1265, 64 USPQ2d 1423, 1429 (Fed. Cir. 2002); Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). Determining that the invention will work for its intended purpose may require testing, depending upon the character of the invention and the problem that it solves. Cooper, 154 F.3d at 1327, 47 USPQ2d at 1901. "The adequacy of a reduction to practice is to be tested by what one of ordinary skill in the art would conclude from the results of the tests." Slip-Track, 304 F.3d at 1265, 64 USPQ2d at 1429, quoting Winter v. Lebourg, 394 F.2d 575, 581, 157 USPQ 574, 578 (CCPA 1968). To prove reduction to practice by inventor testimony, the inventor's testimony must be corroborated by independent evidence. Slip-Track, 304 F.3d at 1265, 64 USPQ2d at 1429; Cooper, 154 F.3d at 1330, 47 USPQ2d at 1903. The corroboration "may consist of testimony of a witness, other than an inventor, to the actual reduction to practice or it may consist of evidence of surrounding facts and circumstances independent of information received from the inventor." Hahn v. Wong, 892 F.2d 1028, 1032-33, 13 USPQ2d 1313, 1317 (Fed. Cir. 1989); Reese v. Hurst, 661 F.2d 1222, 1225, 211 USPQ 936, 940 (CCPA 1981). A reasonableness standard is used to review the sufficiency of corroborating evidence of actual reduction to practice. Scott v.

Finney, 34 F.3d 1058, 1061-62, 32 USPQ2d 1115, 1118 (Fed. Cir. 1994); Holmwood v. Sugavanam, 948 F.2d 1236, 1238, 20 USPQ2d 1712, 1714 (Fed. Cir. 1991). Further, "the standard of proof required to corroborate a reduction to practice, [is] a more stringent standard than that required to corroborate a conception." Singh v. Brake, 222 F.3d 1362, 1369, 55 USPQ2d 1673, 1678 (Fed. Cir. 2000). See Mikus v. Wachtel, 542 F.2d 1157, 1161, 191 USPQ 571, 575 (CCPA 1976) (holding that an invention record, based on an unwitnessed laboratory notebook and results performed by technicians unaware of what they were testing, may provide sufficient evidence of conception but not reduction to practice under the rule of reason).

1. Insufficient corrobation of Nichols' alleged actual reduction to practice

Nichols contends that an experiment begun on (a) April 11, 1994 led to the first corroborated synthesis of a 4-urea derivative within the scope of the Count, i.e., (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxyquinoline methyl ester (NB, p. 33, last ¶). Nichols further contends that the syntheses begun on (b) May 3, 1994, (c) July 1, 1994 and (d) July 13, 1994 all show actual reductions to practice before the June 6, 1997 constructive filing date of Tabakoff (NB, pp. 34-41).

13. At the outset we note that all of the copies of the laboratory notebook pages relied on by Nichols to document Dr. Nichols' synthetic activity, i.e., Exs 2017-2022, 2024, 2030, 2032, 2041-2047, 2049, 2052 and 2072, consist of unsigned and unwitnessed handwritten entries.

14. Dr. Alfred C. Nichols admitted that he alone did all the syntheses recorded in his laboratory notebooks (NR, P. 63, ll. 12-16).[4]

15. According to Dr. Nichols, "[t]he labels I apply to samples correspond to particular samples from particular pages from my Lab Books. Thus, sample 94A-13-III corresponds to sample III from page 13 of my Lab Book No. 94A." (NR, p. 28, ¶ 20).

a. the April 11, 1994 synthesis

16. Dr. Nichols testified that

> [o]n April 11, 1994, ... I utilized triphosgene [$CO(OCCl_3)_2$] to attach the carbonyl group [CO] to the 4-amino group of 4-amino-5,7-dichloro-2-carboxy-quinoline methyl ester and diethylamine [$NH(ethyl)_2$] to attach the secondary amine [N] to the carbonyl group [CO]. Attached as Exhibit 2030 are copies of pages 94A-63 and 94A-64 from my Lab Book documenting this experiment, which also documents the expected product having a 4-diethyl urea substitution. I labeled a sample from this experiment 94A-64-II and had a nuclear magnetic resonance (NMR) spectrum performed on this sample. NMR spectra are used to identify chemical structures. A copy of the spectrum data sheet generated from the NMR spectrum of sample 94A-64-II is attached as Exhibit 2031. The NMR spectral data indicates that the expected product having a 4-diethyl urea substitution ((N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester) was successfully produced. I do not know the exact date that the NMR spectrum was performed; however, page 94A-64 of my Lab Book (Exhibit 2030) includes an entry dated April 28, 1994 relative to the NMR spectrum. [NR, p. 30, ¶ 27.]

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[4] Citations to the testimony of Dr. Nichols are to Nichols Record ("NR") pages, rather than to an exhibit number because Nichols did not submit a complete copy of the November 20, 2001 Deposition of Alfred C. Nichols, Ph.D., as an exhibit. We note that (a) NR pp. 5-16 correspond to Exhibit 2012, pp. 1-12, (b) NR pp. 17-24 correspond to Exhibit 2028, pp. 1-8, (c) NR, pp. 25-37 correspond to Exhibit 2029, ¶¶ 1-61 on unnumbered pp. 1-13, and (d) NR pp. 38, 104, and 105 correspond to Exhibit 1012, a three page document numbered as pp. 1, 67 and 68. Exhibit 2073 is an unsigned, undated thirteen page document titled "Declaration of Alfred C. Nichols" which is identified at NR, p. viii as a draft of Nichols^{3rd} Declaration (related to Exhibit 2029).

17. Notebook Ex 2030 is a two page document that has no notebook identifying number, is improperly dated (year missing), is not signed and is not witnessed.[5]

18. Approximately two-thirds down page 94A-64, Ex 2030 reads "4/28 – NMR; not pure - see too many aromatic carbons – but looks like product is there" (original emphasis).

19. NMR scan Ex 2031 contains the following printout: "94A-64-II; 13C.APY."

20. Ex 2031 has not been authenticated. Neither the test procedure nor the test result shown by the spectral data has been explained.

21. At his deposition, Dr. Nichols backpedaled from his position that Ex 2031 indicated successful production of the theoretically expected product, i.e.,

> A. No, I didn't run the NMR, no.
> Q. Okay. Do you understand what it shows?
> A. To some degree. Ed helped me interpret it, but I was able to see the ethyl peaks. And that showed that at least the diethylamine had been coupled to the quinoline.
> Q. But you couldn't tell where the coupling took place; right?
> A. There was only one place that it could occur.
> Q. But you couldn't tell that from the spectrum?
> A. You can't tell that from any NMR spectra unless you go into much more sophisticated NMR spectroscopy.
> [NR, p. 85, l. 16 - p. 86, l. 9.]

22. Several handwritten notations also appear on Ex 2031, including "have 2 things at least"and "11 quats need only 6."

23. During cross-examination, Dr. Nichols further testified:

> Q. ... there's a handwritten note: Have II things at least. Do you see that?

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[5] To the extent that one or more of Exs 2017-2022, 2024, 2030, 2032, 2041-2047, 2049, 2052 and 2072 do not have a laboratory notebook identifying number on each page thereof, we note that Dr. Nichols brought his laboratory notebooks to his November 20, 2001 deposition, thereby affording Tabakoff the opportunity to examine the original notebooks for identifying numbers (NR, p. 49, l. 21 - p. 50, l. 6).

A. Yes.
Q. That's in your writing, too?
A. Yes.
Q. Same with the eleven quats: Need only six; is that right?
A. Yes.
[NR, p. 90, l. 22 - p. 91, l. 6.]

i. analysis of evidence

Notebook Ex 2030 may well show reactions and products that Dr. Nichols desired and theoretically expected to occur. However, Ex 2030, taken alone, is insufficient to establish that the predicted reactions and theoretically expected products did in fact occur. NMR scan Ex 2031 is of no probative value because it is neither authenticated nor explained. Moreover, Dr. Nichols testified that one could not tell the structure of a compound from its NMR spectrum alone. No other spectral data (e.g., mass spectral or "much more sophisticated NMR" data), etc., have been offered for compound 94A-64-II. Thus, Nichols' alleged synthesis of (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester) rests on the uncorroborated testimony of Dr. Nichols. To prove reduction to practice by inventor testimony, the inventor's testimony must be corroborated by independent evidence. Slip-Track, 304 F.3d at 1265, 64 USPQ2d at 1429; Cooper, 154 F.3d at 1330, 47 USPQ2d at 1903.

In addition, while an inventor need not know that his invention will work for conception to be complete, the discovery that it actually works is part of its reduction to practice. Burroughs Wellcome Co. v. Barr Lab., 40 F.3d 1223, 1228, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994). Here, Nichols has not met its burden of showing that compound 94A-64-II would work for its intended purpose. No anticonvulsant or other pharmacological activity testing has been offered for compound 94A-64-II. Simply

arguing that Nichols "clearly knew that kynurenic acid derivatives had potential use as anticonvulsants" (NB, p. 33, emphasis added) is insufficient to show either that a specific type of kynurenic acid derivative, i.e., a 4-urea derivative, or a specific embodiment thereof, i.e., compound 94A-64-II (a diethyl urea-5,7-dichloro-derivative), would actually work for its intended purpose. (This also applies to compounds 94A-85-I, 94B-27-I and 94B-32-III discussed below.)

Therefore, Nichols fails to meet its burden of proving that the April 11, 1994 experiment resulted in an actual reduction to practice of an embodiment within the scope of the Count, i.e., that the theoretically expected product was obtained and would work for its intended purpose.

b. the May 3, 1994 synthesis

24. Dr. Nichols testified that

> [o]n May 3, 1994, ... I utilized triphosgene [$CO(OCCl_3)_2$] to attach the carbonyl group [CO] to the 4-amino group of 4-tosylamino-5,7-dichloro-2-carboxy-quinoline methyl ester and diethylamine [$NH(ethyl)_2$] to attach the secondary amine [N] to the carbonyl group [CO]. Attached as Exhibit 2032 are copies of pages 94A-81, 94A-83 and 94A-85 from my Lab Book documenting this experiment, which also documents the expected product having a 4-diethyl urea substitution. I labeled a sample from this experiment 94A-85-I.
>
> On May 13, 1994, I had a NMR spectrum performed on sample 94A-85-I. A copy of a spectrum data sheet generated from the NMR spectrum of sample 94A-85-I and the declaration of Edward L. Ezell, the individual who performed the NMR spectrum on sample 94A-85-I, are attached as Exhibit 2034 and Exhibit 2033, respectively. The NMR spectral data indicates that the expected product having a 4-ethyl urea substitution ((N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester) was successfully produced.

> After receiving the NMR results for sample 94A-85-I, I sent a sample of 94A-85-I to the National Institutes of Health (NIH) for anticonvulsant testing. A copy of the NIH registration record and the declaration of James P. Stables, an official of NIH confirming receipt and registration of sample 94A-85-I, are attached as Exhibit 2036 and Exhibit 2035, respectively. The NIH registration record for sample 94A-85-I (Exhibit 2036) includes the date the compound was shipped to NIH (May 13, 1994) and processed by NIH (June 1, 1994) and the chemical structure of the 4-diethyl urea derivative.
> [NR, pp. 30-31, ¶¶ 28-30.]

25. Notebook Ex 2032 is a three page document that has no notebook identifying number, is improperly dated (year missing), is not signed and is not witnessed.

26. The third page of Ex 2032 ("94A-85") contains an elemental analysis entry for sample "85-I" (apparently dated "5/6") having two columns labeled "expected" and "found" and including the comment "elemental analysis off but ratios are close." Dr. Nichols testified that the elemental analysis was done by somebody else (NR, p. 97, ll. 1-10). No copy of the elemental analysis report (authenticated or not) of sample "85-I" is of record.

27. The third page of Ex 2032 (apparently dated "5/13") also contains an entry reading "proton NMR hit – soluble in H_2O & not soluble in acetone – probably sulfate salt (MW = 468)."

28. Edward L. Ezell testified that he performed a proton NMR on a sample designated 94A-85-I provided by Dr. Nichols (NR, p. 176, ¶ 4; p. 185, ll. 18-25).[6]

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[6] Citations to the testimony of Edward L. Ezell are to Nichols Record (NR) pages, rather than to an exhibit number because Nichols did not submit a copy of the November 19, 2001 deposition of Mr. Ezell as a separate exhibit. We note that NR p. 176 corresponds to Ex 2033 (Declaration of Edward L. Ezell).

29. According to Mr. Ezell, Ex 2034 is an accurate copy of the original spectral data generated from sample 94A-85-I (NR, p. 186, ll. 1-23) except that the "chemical structure with '94A-85-I' handwritten thereunder ... was added ... subsequent to its delivery to Dr. Al. Nichols" (NR, p. 176, ¶ 6).

30. Mr. Ezell presumed that Dr. Nichols drew the chemical structure on the data sheet, but did not see him do so (NR, p. 11, ll. 3-17).

31. Dr. Nichols admitted that he made all the handwritten entries on NMR scan Ex 2034 (NR, p. 52, ll. 8-14).

32. Mr. Ezell testified that the "chemical structure drawn on the spectrum data sheet is consistent with the NMR spectrum data" (NR, p. 176,¶ 6).

33. Assuming without determining that the chemical structure of sample 94A-85-I is (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester, the compound would have 17 protons (NR, p. 189, ll. 4-14).

34. At best, Mr. Ezell could only account for 16 of these protons (NR, p. 201, l. 15 - p. 203, l. 7). Mr. Ezell admitted that the 17th proton was not shown on the data sheet, but opined that it was an "exchangeable" hydrogen that "might be exchanging with the water [solvent] too rapidly to see" (Ex 2054; NR, p. 193, ll. 7-18).

35. Mr. Ezell also did not conclusively identify an expected methoxy peak (NR, p. 199, ll. 14-25; p. 200, ll. 13-16; p. 201, ll. 1-13 and p. 203, ll. 12-18).

36. Similarly, Dr. Nichols identified 16 protons from the proton NMR scan but could not conclusively identify the methoxy peak (NR, p. 52, l. 15 - p. 54, l. 21; p. 56, ll. 12-23).

37. Mr. Ezell further testified that proton NMR spectrum, by itself, does not provide enough data to assign a chemical structure to a compound, i.e., additional analytical data was needed (NR, p. 208, ll. 13-21).

38. The third page of Ex 2032 (apparently dated "5/18") contains an entry reading "got good carbon NMR." No copy of the noted carbon NMR (authenticated or not) is of record.

39. The last line of the third page of Ex 2032 is illegible.

40. Dr. Nichols testified that the last line reads "8/2/92 No NIH activity." Dr. Nichols further testified that the date is a mistake, i.e., it should have been "8/2/94." [NR, p. 98, l. 8 - p. 99, l. 16.]

41. Although there is no apparent notation in Ex 2032 documenting sending 250 mg of sample 94A-85-I to NIH for testing, Dr. Nichols testified that such a sample was sent on May 13, 1994 (NR, p. 31, ¶ 30).

42. James P. Stables, Program Director for the NIH Anticonvulsant Project, testified

> Exhibit A is a copy of an Antiepileptic Drug Development (ADD) Registration Record (2 pages) that was received from Dr. Al Nichols and processed by NIH on June 1, 1994. The ADD Registration Record is for the compound identified as 94A-85-I by Dr. Nichols and assigned identification number ADD 234001 by NIH. The ADD Registration Record includes a structural drawing of the compound as provided by Dr. Nichols. [Ex 2035, ¶¶ 2-3].[7]
>
> Exhibit A appears identical to Ex 2036.

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[7] Citation to the direct testimony of Mr. James P. Stables are to Ex 2035 since various exhibits referred to by Mr. Stables are attached thereto. However, citations to cross-examination of Mr. Stables are to Nichols Record ("NR") pages because Nichols did not submit the "Cross-Examination Interrogatories to James P. Stables" as a separate exhibit. We note that NR pp. 214-216 correspond to Ex 2035 sans attached exhibits.

43. The handwritten entries on Ex 2036, including compound identification name, structure, molecular weight and molecular formula, were made by Dr. Nichols. The NIH did not analyze sample 94A-85-I for chemical structure or any other physical property. [NR, p. 100, l. 10 - p. 102, l. 23; pp. 220-221, interrogatory nos. 10-13.]

i. analysis of evidence

Notebook Ex 2032, taken alone, is insufficient to establish that the predicted reactions and theoretically expected products did in fact occur. While the proton NMR data is not inconsistent with the chemical structure drawn by Dr. Nichols thereon (Ex 2034), the proton NMR data alone is insufficient to independently corroborate that sample 94A-85-I is in fact (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester. No additional analytical data, e.g., carbon NMR, mass spectral data, etc. have been offered for sample 94A-85-I. Moreover, even without considerations of the missing/exchangeable 17th proton and inconclusive methoxy peak, Mr. Ezell testified that proton NMR data alone does not provide enough data to assign a chemical structure to a compound. Further, the NIH did not determine the chemical structure or any other physical property of sample 94A-85-I. Thus, none of Exs 2034, 2035 or 2036 (Ex A), alone or in combination, independently corroborate Nichols' alleged synthesis of (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester. Finally, according to Dr. Nichols, sample 94A-85-I did not show anticonvulsant activity in NIH testing.[8]

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[8] In reply to Interrogatory No. 18, i.e., "According to your letter, Exhibit B, the substance tested [by NIH], 94A-85-I (ADD # 00234001), did not exhibit adequate anticonvulsant activity to warrant further testing, is that right?", Mr. Stables replied, "No – only we were not interested in pursuing it" (NR, p. 222). Assuming without determining that sample 94A085-I exhibited de minimus anticonvulsant activity in some unexplained test, Dr. Nichols did not appreciate that sample 94A-85-I would work for its intended purpose as shown by his notation "8/2/92 No NIH activity" (Ex 2032, third page).

Therefore, Nichols fails to meet its burden of proving that the May 3, 1994 experiment resulted in an actual reduction to practice of an embodiment within the scope of the Count, i.e., that the theoretically expected product was obtained and would work for its intended purpose.

c. the July 1, 1994 synthesis

44. Dr. Nichols testified that

> [o]n July 1, 1994, I ... utilized triphosgene [$CO(OCCl_3)_2$] to attach the carbonyl group [CO] to the 4-amino group of 4-tosylamino-5,7-dichloro-2-carboxy-quinoline ethyl ester and diethylamine [$NH(ethyl)_2$] to attach the secondary amine [N] to the carbonyl group [CO]. Previously filed as Exhibit 2022 are copies of pages 94B-20 and 94B-27 from my Lab Book documenting this experiment. I labeled a sample from this experiment 94B-27-I.
>
> On July 22, 1994, I sent 100 mg of 94B-27-I ((N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester) to Snell for pharmacological testing and 300 mg to NIH (NIH # 236001) for anticonvulsant testing (see page 94B-27-I from Exhibit 2022). A copy of the NIH registration record for sample 94B-27-I is attached as Exhibit 2037 to the declaration of James P. Stables (Exhibit 2035). The NIH registration record for sample 94B-27-I (Exhibit 2037) includes the date the compound was shipped to NIH (July 22, 1994) and processed by NIH (August 1, 1994) and the chemical structure of the 4-diethyl urea derivative. Previously filed as Exhibit 2023 are test results from NIH dated August 31, 1994 for sample 94B-27-I.
> [NR, p. 32, ¶¶ 34-35.] [See also NR, p. 14, ¶¶ 43-44.]

45. Notebook Ex 2022 is a two page document which contains no readable page number on the first page. About three-quarters down the first page appears "7/5" with no year given. The last entry on the first page is "did reaction go??". The top of the second page is numbered "027", dated "7/15/94," and contains the entry "from page 23". Neither page is signed nor witnessed. Page 94A-23 is not of record.

46. The second page of Ex 2022 ("94A-27") contains a drawing of (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester) labeled as "23-III" and an elemental analysis entry for sample 23-III having several crossed out columns and one column labeled "found." Dr. Nichols testified that he recorded the elemental values from the company that did the elemental analysis on sample 23-III and that he himself did not perform the analysis (NR, p. 109, l. 7 - p. 110, l. 12). No copy of the elemental analysis report (authenticated or not) of sample "85-I" is of record.

47. Mr. Stables testified that

> ...Exhibit C is a copy of an Antiepileptic Drug Development (ADD) Registration Record (2 pages) that was received from Dr. Al Nichols and processed by NIH on August 1, 1994. The ADD Registration Record is for the compound identified as 94B-27-I by Dr. Nichols and assigned identification number ADD 236001 by NIH. The ADD Registration Record includes a structural drawing of the compound as provided by Dr. Nichols. [Ex 2035, ¶ 5.]
>
> Exhibit C appears identical to Exhibit 2037.

48. The handwritten entries on Ex 2037, including compound identification name, structure, molecular weight and molecular formula, were made by Dr. Nichols. The NIH did not analyze sample 94B-27-I for chemical structure or any other physical property. [NR, p. 113, ll. 9-14; pp. 223-224, interrogatory nos. 21-23.]

49. Mr. Stables also testified that he sent Dr. Nichols a letter dated September 2, 1994 in reference to ADD 236001, a copy of which is Exhibit D (Ex 2035, ¶ 6). In that letter (Ex D), Mr. Stables indicated that a TTE test was being implemented at the NIH in hopes of finding compounds which are significantly active in the "new" TTE test but devoid of activity in the "traditional" MES test to see if such compounds may represent

substances acting by different mechanisms of action.

50. Dr. Nichols testified that a test report accompanied the September 2, 1994 letter (Ex D) (NR, p. 111, ll. 7-19), which report has been identified as Ex 2059.

51. The NIH test report Ex 2059 is a two page document containing MES and TTE test data for ADD 236001, respectively. The MES data page has a handwritten entry "94B-27-I." The TTE data page has a handwritten circle drawn around the column under 2 hours and a handwritten chemical structure labeled 94B-27-I at the bottom.

52. The handwritten entries on Ex 2059 were made by Dr. Nichols (NR, p. 112, l. 11 - p. 113, l. 8).

53. Neither test procedure, i.e., MES or TTE, nor its test results has been explained. At best, Mr. Stables indicated in the September 2, 1994 letter (Ex D) that although ADD 236001 was active at 2 hours in the TTE test, the activity was not potent enough to warrant further study.

Dr. Nichols stated that he sent 100 mg of sample 94B-27-I to Dr. Snell for "pharmacological" testing. However, Nichols has not pointed to, and we do not find, where evidence of the exact nature and results of such "pharmacological" testing of sample 94B-27-I by Dr. Snell is of record.

i. analysis of evidence

Notebook Ex 2022, taken alone, is insufficient to establish that the predicted reactions and theoretically expected products did in fact occur. It appears that an intervening page, i.e., 94B-23, should have been included in Ex 2022 given the reference to page 23 on the second page of Ex 2022 and the reference to sample "23-

III." No additional analytical data, e.g., NMR, mass spectral data, etc. have been offered for sample 94B-27-I. Further, the NIH did not determine the chemical structure or any other physical property of sample 94B-27-I. Thus, none of Exs 2035, 2037 (Ex C), 2059 or D, alone or in combination, independently corroborate Nichols' alleged synthesis of (N,N-diethyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester. Moreover, neither Exs 2059 or D, alone or in combination, are sufficient to show that sample 94B-27-I would work for its intended purpose, especially given that the TTE test is "new" and neither the test procedure nor the significance of its results have been explained.

Therefore, Nichols fails to meet its burden of proving that the July 1, 1994 experiment resulted in an actual reduction to practice of an embodiment within the scope of the Count, i.e., that the theoretically expected product was obtained and would work for its intended purpose.

d. the July 13, 1994 synthesis

54. Dr. Nichols testified that

> [o]n July 13, 1994, ... I utilized triphosgene [$CO(OCCl_3)_2$] to attach the carbonyl group [CO] to the 4-amino group of 4-tosylamino-5,7-dichloro-2-carboxy-quinoline ethyl ester and diphenylamine [$NH(diphenyl)_2$] to attach the secondary amine [N] to the carbonyl group [CO]. Previously filed as Exhibit 2024 are copies of pages 94B-25 and 94B-32 from my Lab Book documenting this experiment. I labeled a sample from this experiment 94B-32-III.
>
> I sent a sample of 94B-32-III for mass spectral analysis. On August 10, 1994, a fast atom bombardment (FAB) mass spectrum was performed in the Analytical Chemistry Center of the University of Texas Medical School in Houston on 94B-32-III. A copy of a spectrum data sheet generated from the FAB spectrum of 94B-32-III and the declaration of William E. Seifert, Assistant Director of the Analytical Chemistry Center in August

> 1994, are attached as Exhibit 2039 and Exhibit 2038, respectively. The mass spectral data indicates that the expected product having a 4-diphenyl urea substitution ((N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester) was successfully produced.
>
> On August 12, 1994, I sent 10 mg of 94B-32-III ((N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester) to Snell for pharmacological testing and 280 mg to NIH (NIH # 236075) for anticonvulsant testing (see page 94B-32 from Exhibit 2024). Snell references this compound in his email addressed to me dated July 10, 1996, previously filed as Exhibit 2026. A copy of the NIH registration record for sample 94B-32-III is attached as Exhibit 2040 to the declaration of James P. Stables (Exhibit 2035). The NIH registration record for sample 94B-32-III (Exhibit 2040) includes the date the compound was shipped to NIH (August 12, 1994) and processed by NIH (August 30, 1994) and the chemical structure of the 4-diphenyl urea derivative.
> [NR, p. 33, ¶¶ 36-38.] [See also NR, p. 14, ¶¶ 45-46.]

55. Notebook Ex 2024 is a two page document that has no notebook identifying number on either page, is improperly dated (year missing), is not signed and is not witnessed.

56. The second page of Ex 2024 contains an entry, reading in relevant part, "8/4 have NMR that seems to fit ... 8/12 mass spectrum: 479 & 481 got great mass spectrum." No copy of the NMR spectral data (authenticated or not) referred to in Ex 2024 is of record.

57. William E. Seifert, Jr., Ph.D., testified that he performed a FAB mass spectrum on a sample designated 94B-32-III provided by Dr. Nichols (NR, p. 241, ¶ 4).[9]

58. The FAB mass spectral data obtained for 94B-32-III is shown in Ex 2039.

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[9] Citations to the testimony of Dr. Seifert are to Nichols Record (NR) pages because Nichols did not submit a copy of the November 19, 2001 Oral Deposition of Dr. Seifert as an exhibit. We note that NR p. 241 corresponds to Ex 2038.

59. Mass spectrum Ex 2039 is a two page document consisting of a fax cover sheet and a FAB mass spectral data sheet, listed as pages 001 and 003 in the top fax transmission line, respectively. The fax purports to be a five page document.[10] Dr. Seifert does not know where the presumed other three fax pages are or what they contained (NR, p. 259, l. 2 - p. 260, l. 3).

60. The second page of Ex 2039 contains three hand-written notations. Dr. Seifert testified that two (i.e., the "[M+H]" note above the "mass 480.1" and the arrow going from the peak at 480.1 to the peak at 44.2 with the designation minus HCl) were made by him when he analyzed the spectrum in 1994 (NR, p. 256, ll. 2- 22). Dr. Seifert presumed that Dr. Nichols added the third notation, a chemical structure, to the top of the data sheet after Seifert had made his notations (NR, p. 256, l. 23 - p. 257, l. 11).

61. According to Dr. Seifert, while FAB mass spectra are used to help identify chemical structures (NR, p. 241, ¶ 4), FAB mass spectra by themselves do not identify chemical structure (NR, p. 257, ll. 12-14). For example, the same FAB mass spectrum would be obtained from the chemical structure written on Ex 2039 as from a chemical structure in which the ethyl group and the diphenylimino group were reversed (NR, p. 257, ll. 15-22).

62. Nichols was asked at final hearing which one or more of Dr. Nichols' lab notebook, the FAB mass spectral data of 94B-32-III or submission reports of 94B-32-III to Mr. Stables established the actual, not theoretical, structure of 94B-32-III (Transcript,

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[10] Exhibit 2060 is purportedly Dr. Nichols' copy of the Seifert fax (Ex 2039). Fax Ex 2060 is a four page document with pages 001, 003, 004 and 005 indicated in the top fax transmission lines of each page. Dr. Nichols does not have the missing page (NR p. 117, l. 1 - p. 118, l. 5). It does not appear as if Dr. Seifert was shown Ex 2060, e.g., to authenticate Ex 2060 or to refresh his memory of Ex 2039.

Paper 107, p. 12, ll. 6-22). Nichols stated that the lab notebook (Ex 2024) "obviously is not proof of that that [94B-32-III] was synthesized" (id., p. 13, ll. 1-6). Nichols further stated that "...what Dr. Seifert testified was that the [diphenyl] structure that was [subsequently] drawn [by Dr. Nichols] on the sheet was consistent with the mass spectral data. So it's indicative that that product was actually synthesized" (id., p. 14, ll. 6-19). However, when it was put to Nichols that "what he [Dr. Seifert] said was that the mass spec data was consistent with the structure or that the structure was not inconsistent with the data. But he did not say that spectra [sic] is that structure" (id., p. 14, l. 20 - p. 15, l. 2), Nichols replied "That's correct. But he did say that there's only so many structures that it could be" (id., p. 15, ll. 3-5) (see also id., p. 18, ll. 7-19). When asked if Dr. Seifert gave any indication of about how many possible structures there were, Nichols replied "[w]hat they were specifically talking about was one other possibility. They did not go into questioning how may possibilities there were." (id., p. 15, l. 6 - p. 16, l. 3). As to that at least one other structure, Nichols stated that it would be outside the interference count (id., 16, l. 7 - p. 17, l. 10). Finally, Nichols stated that the NIH submission Exs 2040 and E (Ex 2035) "showed that at the time it [94B-32-III] was submitted to NIH, Dr. Nichols did believe that that was what the structure was. And that was based on the mass spectral data" (id., p. 17, l. 13 - p. 18, l. 6).

63. Mr. Stables testified that

> ... Exhibit E is a copy of an Antiepileptic Drug Development (ADD) Registration Record (2 pages) that was received from Dr. Al Nichols and processed by NIH on August 30, 1994. The ADD Registration Record is for the compound identified as 94B-32-III by Dr. Nichols and assigned identification number ADD 236075 by NIH. The ADD Registration Record includes a structural drawing of the compound as provided by Dr. Nichols.

[Ex 2035, ¶ 7.]

Exhibit E appears identical to Exhibit 2040.

64. The handwritten entries on Ex 2040, including compound identification number, structure, molecular weight and molecular formula, were not made by Mr. Stables. The NIH did not analyze sample 94B-32-III for chemical structure or any other physical property. [NR, pp. 226-227, interrogatory nos. 31-33.]

65. Mr. Stables further testified that "... Exhibit F is a copy of a letter dated October 13, 1994 to Dr. Al Nichols from NIH and signed by me in reference to ... ADD 236075" (Ex 2035, ¶ 8).

66. Mr. Stables still further testified that ADD 236075, i.e., compound 94B-32-III, did not exhibit adequate anticonvulsant activity to warrant further testing (NR, p. 228, interrogatory no. 38).

67. Dr. Nichols testified that he sent 10 mg of 94B-32-III to Dr. Snell on August 12, 1994 for "pharmacological" testing. However, Nichols has not pointed to, and we do not find, where evidence of the exact nature and results of such "pharmacological" testing of sample 94B-32-III by Dr. Snell is of record.[11]

i. analysis of evidence

Notebook Ex 2024, taken alone, is insufficient to establish that the predicted reactions and theoretically expected products did in fact occur. Further, as testified by

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[11] According to e-mail Ex 2026, sent almost two years later, Dr. Snell asked Dr. Nichols for any copies of MES, PTZ and toxicity data that he might have for the ethyl ester form of compound 94B-80-I or 95A-1-II, which ethyl ester form was termed "94B-32-III." Assuming without determining that sample 94B-32-III is the ethyl ester form of a compound with a later identifying label, Ex 2026 neither acknowledges receipt of sample 94B-32-III by Dr. Snell on August 12, 1994 nor sheds any light on any "pharmacological" testing he might have performed on the purported August 12, 1994 sample.

Dr. Seifert and acknowledged by Nichols, while the FAB mass spectrum is not inconsistent with the chemical structure drawn by Dr. Nichols, the FAB mass spectrum data alone is insufficient to independently corroborate that sample 94B-32-III is in fact (N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester. No additional data, e.g., NMR data, etc. have been offered for sample 94B-32-III. Further, the NIH did not determine the chemical structure or any other physical property of sample 94B-32-III. Thus, none of Exs 2035, 2039, 2040 (Ex E) or F, alone or in combination, independently corroborate Nichols' alleged synthesis of (N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline ethyl ester. Additionally, Ex F is inconclusive as to whether sample 94B-32-III would work for its intended purpose.

Therefore, Nichols fails to meet its burden of proving that the July 13, 1994 experiment resulted in an actual reduction to practice of an embodiment within the scope of the Count, i.e., that the theoretically expected product was obtained and would work for its intended purpose.

In summary, Nichols fails to meet its burden of proving that any of its experiments begun on (a) April 11, 1994, (b) May 3, 1994, (c) July 1, 1994 or (d) July 13, 1994 resulted in an actual reduction to practice of an embodiment within the scope of the Count before Tabakoff's June 6, 1997 effective filing date.

B. Derivation

Notwithstanding the failure to prove an actual reduction to practice, Nichols may still prevail if it can prove that Tabakoff derived the subject matter of the invention from Nichols.

"The issue of derivation is one of fact and the party asserting derivation has the burden of proof... . Derivation is shown by a prior, complete conception of the claimed subject matter and communication of the complete conception to the party charged with the derivation." Hedgewick v. Akers, 497 F.2d 905, 908, 182 USPQ 167, 169 (CCPA 1974). In Gambro Lundia AB v. Baxter Healthcare Corp., 110 F.3d 1573, 1578, 42 USPQ2d 1378, 1383 (Fed. Cir. 1997), the court held that the "correct standard" for derivation is "whether the communication enabled one of ordinary skill in the art to make the patented invention."

Nichols contends that Tabakoff's request to Dr. Nichols to synthesize a 4-urea kynurenic acid derivative was simply a research plan because Tabakoff did not suggest a specific chemical structure for the derivative or a synthesis method therefor. Nichols alleges that "extensive" research was required to obtain an operable synthesis method. [NB, pp. 28-30.] Nichols relies on a March 23, 1994 experiment recorded in Dr. Nichols' lab notebook (Ex 2020) to show complete conception, i.e., "knowledge of both the specific chemical structure of the compound and an operative method of making it" (id., p. 32). Nichols further contends that it communicated that information to Tabakoff as shown in letters and e-mails from Tabakoff acknowledging Nichols as "the entity responsible for the synthesis of these compounds" (id., p. 25).

Tabakoff argues that none of the evidence shows that Nichols knew of or had made any 4-urea kynurenic acid derivatives before Dr. Snell requested Dr. Nichols to make such compounds. Tabakoff further argues that Dr. Snell sent scientific publications to Dr. Nichols on the synthesis of similar types of prior art compounds.

Tabakoff still further argues that Nichols has misconstrued polite acknowledgments in correspondence by Dr. Tabakoff that Dr. Nichols performed routine experiments and synthetic activities that should inure to Tabakoff's benefit. [TO, pp. 35-37.]

1. conception

"Conception is the formation 'in the mind of the inventor of a definite and permanent idea of the complete and operative invention, as it is therefore to be applied in practice and a conception must encompass all limitations of the claimed invention.'" Kridl v. McCormick, 105 F.3d 1446, 1449, 41 USPQ2d 1686, 1689 (Fed. Cir. 1997). Conception "is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." Burroughs, 40 F.3d at 1228, 32 USPQ2d at 1919. Furthermore, a party must provide independent corroboration for his alleged conception. Reese v. Hurst, 661 F.2d 1222, 1225, 211 USPQ 936, 940 (CCPA 1981). There is no particular formula that an inventor must follow in providing corroboration of his testimony of conception. Kridl, 105 F.3d at 1450, 41 USPQ2d at 1689. Rather, whether a putative inventor's testimony has been sufficiently corroborated is determined by a "rule of reason" analysis, in which "an evaluation of all pertinent evidence must be made so that a sound determination of the credibility of the inventor's story may be reached." Price, 988 F.2d at 1195, 26 USPQ2d at 1037. However, that "rule of reason" analysis does not alter the requirement of corroboration of an inventor's testimony. Brown v. Barbacid, 276 F.3d 1327, 1335, 61 USPQ2d 1236, 1240 (Fed. Cir. 2002). Since conception is a mental act, "it must be proved by evidence showing what the

inventor has disclosed to others and what that disclosure means to one of ordinary skill in the art." In re Jolley, 308 F.3d 1317, 1321, 64 USPQ2d 1901, 1904 (Fed. Cir. 2002), quoting Spero v. Ringold, 377 F.2d 652, 660, 153 USPQ 726, 732 (CCPA 1967). The evidence must show that the inventor disclosed to others his "completed thought expressed in such clear terms as to enable those skilled in the art" to make the invention. Coleman v. Dines, 754 F.2d 353, 359, 224 USPQ 857, 862 (Fed. Cir. 1985); Field v. Knowles, 183 F.2d 593, 600, 86 USPQ 373, 379 (CCPA 1950).

a. the chemical structure of a 4-urea kynurenic acid derivative originated with Tabakoff

68. Initially, we note, by way of background, that Dr. Nichols testified that

> [m]y research with NMDA receptors and antagonists led to my work with kynurenic acid derivatives. Kynurenic acid derivatives have been shown to be a competitive inhibitor [sic] of glycine binding at the NMDA receptor. Unless specifically stated otherwise, any references in this declaration to my work in designing and synthesizing novel kynurenic acid derivatives involved the inventive contributions of K. Lemone Yielding ("Yielding").
>
> * * * * * *
>
> Continuing research with kynurenic acid derivatives led to the syntheses of novel 4-amino substituted derivatives for use as NMDA antagonists, such as 4-methylamino-5,7-dichloro-2-quinoline carboxylate, which became the subject of U.S. Patent No. 5,493,027, issued in 1996 [based on application 6,918, filed January 22, 1993] (previously filed as Exhibit 2015).
>
> [NR, pp. 25-26, ¶¶ 6, 8.]

69. Dr. Nichols testified that he met Larry Snell (one of the Tabakoff inventors), then a Ph.D. graduate student studying the pharmacology of NMDA receptors, while working at the University of Texas Medical Branch (NR, p. 6, ¶ 10; p. 26, ¶ 9).

70. Dr. Snell joined Dr. Boris Tabakoff at the University of Colorado following his Ph.D. and postdoctoral studies (NR, p. 10, ¶ 24; p. 26, ¶ 10).

71. After joining Dr. Tabakoff, Dr. Snell contacted Dr. Nichols in December 1993 or January 1994 and requested him to make a 4-urea kynurenic acid derivative because Dr. Snell wanted to study the efficacy of this compound in treating alcohol withdrawal (NR, pp. 10-11, ¶¶ 25-26; p. 26, ¶ 10).[12]

First, Nichols does not present any evidence that it knew of any **4-urea** kynurenic acid derivative, within or without the Count, let alone any specific chemical structure of such a derivative, e.g., one having a disubstituted urea group, prior to being asked to make 4-urea derivatives by Dr. Snell in December 1993 or January 1994. Second, an unsubstituted 4-urea derivative (i.e., a compound according to Nichols claim 1 or 15 wherein R_1, R_2, R_3, X_1, X_2, X_3 and X_4 are all hydrogen), is a specific chemical structure which is clearly within the scope of the Count, whereas a **4-amino** kynurenic acid derivative, as previously studied by Nichols, is not. Third, Nichols has not argued that a particular type of derivative, e.g., a 4-urea kynurenic acid having a disubstituted urea group, is required to meet all the limitations of the Count.

Thus, conception of a 4-urea kynurenic acid derivative would have been complete in Tabakoff's mind if it was within ordinary skill in the art to synthesize a 4-urea kynurenic acid derivative.

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[12] Exhibit 2056 is a single-page fax cover page bearing the date of December 9, 1993 addressed from Dr. Snell to Dr. Nichols. Exhibit 2057 is a single-page document showing three specific chemical structures. Neither exhibit has been authenticated. Dr. Nichols expressly testified that he did not remember receiving fax Ex 2056 or a request concerning the particular structures of Ex 2057. [NR, p. 71, l. 14 - p. 72, l. 22.] Therefore, neither Ex 2056 nor 2057 has been accorded any weight or relied upon.

b. Nichols fails to establish that "extensive" or "undue" experimentation was required to synthesize a 4-urea kynurenic acid derivative

Nichols argues that conception requires knowledge of both the specific chemical structure of the compound and an operative method of making it (NR, p. 29, ¶ 3) and that it required "extensive" research to determine whether a 4-urea kynurenate derivative could actually be synthesized (id., p. 30, ¶ 2). According to Nichols, it "attempted several experiments over several months using 2 synthetic schemes that were unsuccessful before it conceived of a new synthetic scheme which subsequently proved successful" (NB, p. 30).

"The test [for extensive or undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine...." PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) (quotation and citation omitted); see also In re Wands, 858 F.2d 731, 736-40, 8 USPQ2d 1400, 1403-07 (Fed. Cir. 1988). The determination of what constitutes undue experimentation in a given case must be decided on the facts of each particular case and requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art.

In its reply brief, Nichols asks "[w]here is Party Tabakoff's evidence that Party Nichols' synthetic skills were only 'ordinary'?" (NRB, p. 17). That is precisely the wrong question. It is Nichols' burden to show by a preponderance of the evidence that synthesis of 4-urea kynurenates required undue experimentation.

However, there is no testimony by anyone other than Dr. Nichols himself that it was not within ordinary skill in the art to synthesize 4-urea kynurenate derivatives, after Dr. Snell's disclosure of these compounds. Moreover, the facts do not lend much support to Dr. Nichols' opinion that undue or extensive research was required to determine whether a 4-urea kynurenate derivative could actually be synthesized.

72. Dr. Nichols is not an organic chemist (NR, p. 6, ¶¶ 3-7). According to Dr. Nichols, his "work in designing and synthesizing novel kynurenic acid derivatives involved the inventive contributions of K. Lemone Yielding" (NR, pp. 9-10).

73. During cross-examination, Dr. Nichols explained the inventive contributions of Dr. Yielding as

> A. He and I just set design compounds together and discussed what we would do with them, what might be the best way to synthesize them, what questions we could investigate by producing these types of compounds.
>
> Q. Do you recall any specific inventive contribution that Dr. Yielding made?
>
> A. Oh, definitely. He and I talked about doing this on at least a weekly basis, sometimes more often. It's -- we interact on what we were going to do and why, and possible ways to do it.
>
> Q. Now, did he contribute to a particular compound?
>
> A. He made -- He contributed to how best to do the syntheses and what experiments we would undertake to show that the products are doing what we want them to do. We interact regularly. I can't -- I can't think of how he would no -- We just interact as coworkers. Bounce ideas, procedures, techniques off of each other.
> [NR, p. 30, l. 9 - p. 31, l. 9.]

There is no evidence that Dr. Nichols discussed any unusual or unexpected synthesis problems, approaches, etc. with Dr. Yielding. Dr. Yielding is silent as to whether he

considered synthesis of 4-urea kynurenic acid derivatives within or beyond ordinary skill in the art.[13] Nichols did not offer any independent testimony by one of ordinary skill in the art sharing Dr. Nichols' opinion that undue or extensive research was required to synthesize 4-urea kynurenate derivatives. Nichols has not pointed to, and we do not find, evidence that Dr. Nichols had to undertake extensive literature searches, scientific consultations, etc. as to possible synthesis routes.

74. To the contrary, Dr. Nichols admitted that Dr. Snell sent him papers on synthesizing similar types of prior art compounds (NR, p. 72, l. 23 - p. 73, l. 22).

75. Moreover, according to James A. Ruth, a Ph.D. in synthetic organic chemistry who testified on behalf of Tabakoff, an ordinary organic chemist would have known how to synthesize a 4-urea kynurenic acid, e.g.,

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[13] The Declaration of Dr. K. Lemone Yielding (Ex 2001; NR, pp. 1-2) is confined to authenticating six letters (Exs 2003-2007) he received from Dr. Tabakoff.

Method step	as described in the following prior art
(1) react aniline with a dialkyl acetylenedicarboxylate,	Harrison et al. ("Harrison"), J. Med. Chem., 33:3130-3132 (1990) (Ex 1003), p. 3132, Scheme I, step (a).
(2) cyclize the product of (1) to form an alkyl ester of kynurenic acid	Harrison, Ex 1003, p. 3132, Scheme I, step (b).
(3) aminate the alkyl ester of (2) with an isocyanate to form a 4-aminated derivative, and	Wright, Synthesis, 1984 (12):1058-1061 (Ex 1004), pp. 1058-1059.
(4) acylate the 4-aminated derivative of (3) with triphosgene and a secondary amine to produce a 4-urea-2-quinoline alkyl carboxylate.	Leeson et al. ("Leeson"), J. Med. Chem., 34(11):1954-1968 (1992) (Ex 2016) at p. 1956 where reaction with phosgene is shown in step (c) of Scheme V. also Degering, Organic Chemistry, 6th ed., Barnes & Noble, Inc., New York (1957) (Ex 1008), p. 139 or March, Advanced Organic Chemistry, 4th ed., John Wiley & Sons, Inc., New York (1992) (Ex 1009), pp. 417-418

[Ex 1007, ¶¶ 7-14.]

76. Not surprisingly, Dr. Nichols disagrees with Dr. Ruth's opinion and interpretation of the prior art (NR, pp. 18-21, ¶¶ 4-19). (Dr. Ruth was not cross-examined.)

77. We find that Dr. Ruth's testimony is entitled to more weight than Dr. Nichols' testimony. To the extent there is a conflict, we accept the testimony of Dr. Ruth and reject that of Dr. Nichols. Dr. Ruth is an organic chemist; Dr. Nichols is not. Moreover, Dr. Ruth's testimony is consistent with the fact that Nichols' synthesis method included organic synthesis steps described in the prior art, e.g., Harrison, Wright, Leeson and March, and with well-known principles of organic chemistry, e.g., aromatic and aliphatic compounds may have different chemical reactivities.

78. Furthermore, although Dr. Nichols testified that he did not remember Leeson (Ex 2016) being among the synthesis papers sent to him by Dr. Snell (NR, p. 72, l. 23 - p. 73, l. 12), Dr. Nichols testified that he used Leeson as the starting point for his synthetic scheme (NR, p. 27, ¶¶ 28-29; p. 27, ¶¶ 13-14).

79. In particular, Dr. Nichols testified that he had seen a similar compound described in a paper by Leeson entitled "4-Amido-2-carboxytetrahydroquinolines. Structure-Activity Relationships for Antagonism at the Glycine Site of the NMDA Receptor." (Ex 2016). Leeson disclosed seven different synthetic schemes (id., pp. 1954-1956). For example, Leeson prepared "[u]reas ... from reactions of 66 [2-carboxy-5,7-dichloro-4-amidotetrahydroquinoline] with the appropriate isocyanates" (id., p. 1955, c. 1).

80. According to Dr. Nichols,

> The compounds synthesized by Leeson substitute a urea compound onto saturated [i.e., aliphatic] rings, whereas the synthesis method of the present invention substitutes a urea compound onto an unsaturated [i.e., aromatic] ring. Based on our long experience of working in the lab with kynurenates, I can attest that kynurenates behave both chemically and biologically different from the tetrahydroquinoline counterparts utilized Leeson. The 4-amino group in the kynurenate compound exists as a tautomer with the ring nitrogen, making it unreactive with the isocyanates used by Leeson. This is why, as stated in my prior declaration, the reaction used by Leeson to synthesize 4-urea substituted tetrahydroquinoline derivatives was not effective in synthesizing the compounds of this interference. Exh. 2012, ¶ 30. [NR, p. 20, ¶ 12.]

In other words, Dr. Nichols appears to think an isocyanate might not react with a 4-amino-2-carboxyquinoline.

81. Nonetheless, on (a) January 20 and (b) February 3, 1994, Dr. Nichols attempted his first synthetic scheme, i.e., reacting isocyanate with the 4-amino group of two aromatic ring compounds, i.e., (i) 4-amino-5,7-dichloro-2-carboxyquinoline methyl ester

and (ii) 4-amino-7-chloro-2-carboxyquinoline methyl ester, respectively, to make 4-urea derivatives thereof. Dr. Nichols testified that Exs 2017 and 2019 are copies of his lab notebooks documenting these experiments, i.e., (a) page 94A-2 and (b) page 94A-14, respectively. Dr. Nichols further testified that neither experiment produced the desired product. [NR, pp. 11-12, ¶¶ 30, 33, 36; pp. 27-28, ¶¶ 15, 18.] Dr. Nichols did not state how or when he determined that the desired product was not produced.

82. On (c) January 20 and (d) January 28, 1994, Dr. Nichols attempted his second synthetic scheme, i.e., reacting urea with the 4-amino group of (i) 4-amino-5,7-dichloro-2-carboxyquinoline methyl ester and (ii) 4-amino-7-chloro-2-carboxyquinoline methyl ester, respectively, to make 4-urea derivatives thereof. Dr. Nichols testified that Exs 2017 and 2018 are copies of his lab notebook pages documenting these experiments, i.e., (c) page 94A-2 and (d) page 94A-11. Dr. Nichols testified that neither experiment produced the desired product. [NR, p. 12, ¶¶ 31-32, 36; p. 28, ¶¶ 16-17, 21.] Dr. Nichols did not state how or when he determined that the desired product was not produced.

83. On February 9, 1994, Dr. Nichols combined samples from the experiments reacting (ii) 4-amino-7-chloro-2-carboxyquinoline methyl ester with (b) isocyanate or (d) urea and sent 52 mg of the combined sample labeled as 94A-13-III to Dr. Snell (Tabakoff) (Ex 2017, p. 013; NR, p. 12, ¶ 34; p. 28, ¶ 19).

84. On February 16, 1994, Dr. Nichols received results NMR data showing that the combined sample did not contain the desired product. He then either called or e-mailed Dr. Snell to tell him that 94A-13-III was the 4-amino, not 4-urea, derivative (NR, p. 75, l.

12 - p. 76, l. 15). Notebook Ex 2018 contains an entry "2/16 NMR shows [4-amino-7-chloro-2-quinoline carboxylic acid structure] so does MS."

85. It appears that Dr. Nichols conceived of his third synthetic scheme "[o]n or before about February 15, 1994" (NR, p. 29, ¶ 24), before he knew for sure that schemes one and two did not work. To wit,

> [o]n or about February 15, 1994, ... [Dr. Nichols] decided that phosgene [$COCl_2$] may be reactive enough to attach its acyl carbon to the 4-amino group of the 4-amino-2-carboxylic-quinoline compound, after which, ... [he] would attempt to attach a secondary amine [N] to the carbonyl group [CO] because it was a stronger Lewis base and (2) there was not a risk of it forming a dimer with another quinoline structure. ... [NR, p. 29, ¶ 24.]

86. Dr. Nichols already had diethylamine in his laboratory. He substituted triphosgene for phosgene when he found out that triphosgene was commercially available whereas phosgene was not. Dr. Nichols ordered triphosgene from Aldrich Chemical Company. [NR, p. 13, ¶ 38; p. 29, ¶¶ 24-25.]

87. We note for the record that Dr. Ruth testified that "phosgene (an acyl halide) and triphosgene are equivalent" for this acylation reaction, citing "Aldrich Catalog Handbook of Fine Chemicals 1994-1995, p. 1427 (Tabakoff Exhibit 1010)" (Ex 1007, p. 5, ¶ 15). We also note that March discloses "[w]hen phosgene is the acyl halide, both aliphatic and aromatic primary amines give chloroformamides ClCONHR that lose HCl to give isocyanates RNCO" (Ex 1009, p. 418). Thus, it appears that triphosgene would have been expected to acylate either an aliphatic or aromatic primary amine.

88. According to Dr. Nichols and his notebook Ex 2020, 4-amino-7-chloro-2-quinoline carboxylate was made on March 23, 1994. That 4-amino compound was reacted with triphosgene, followed by diethylamine on March 27, 1994. However,

according to Dr. Nichols, the theoretically expected 4-urea product could not be isolated from this experiment. [Ex 2018; NR, p. 13, ¶ 39; pp. 29-30, ¶ 26; p. 79, l. 16 - p. 82, l. 11.]

Nichols argues that "[a]lthough Dr. Nichols was unable to successfully isolate the expected product, his documentation of this [March 23, 1994 synthesis] experiment clearly supports the Junior Party's knowledge of both the specific chemical structure of the compound and an operative method of making it" (NB, p. 32, ¶ 1).

89. It is Nichols' position that "Dr. Nichols' lab notebooks alone are adequate to corroborate his testimony of conception" (NRB, p. 6, ¶ 3).

However, the same may be said of Dr. Nichols' lab notebooks alone vis-a-vis Nichols' first two "inoperable" synthetic schemes.

90. Next follows Dr. Nichols' (a) April 11, 1994, (b) May 3, 1994, (c) July 1, 1994 and (d) July 13, 1994 experiments discussed above.

In summary, the evidence suggests that Dr. Nichols (i) attempted two synthetic schemes on two days, January 20, 1994 and February 3, 1994, (ii) thought of a third "operable" synthetic scheme on February 15, 1994, seemingly as a matter of course, before, (iii) he found out that the first two schemes did not yield the expected product on February 16, 1994 and (iv) began his first allegedly successful synthesis on March 23, 1994 because he had to wait for a triphosgene reagent ordered from Aldrich Chemical Company to arrive. The evidence further suggests that Dr. Nichols knew that aliphatic and aromatic compounds differ in their chemical reactivity and that the prior art recognized that phosgene reacts with both aliphatic and aromatic primary amines and

that phosgene and triphosgene are equivalent for this type of acylation reaction. The evidence still further suggests that the particular 4-urea derivative synthesized was determined, at least in part, by what chemicals Dr. Nichols already had in his laboratory. The evidence does not suggest extensive experimentation or research over an extensive time period prior to conception of Dr. Nichols' "operable" synthetic scheme. Thus, we do not find credible the testimony of Dr. Nichols that "extensive experimentation" beyond ordinary skill in the art was required to synthesize 4-urea kynurenic acid derivatives in view of the above and the testimony of Dr. Ruth.

Therefore, since the chemical structure of the subject matter of the Count originated with Tabakoff and since Nichols fails to show by a preponderance of the evidence that synthesis of 4-urea kynurenates required undue experimentation, Nichols fails to establish conception of the subject matter of the Count.

2. communication

To prove derivation, Nichols must establish prior conception of the claimed subject matter and communication of the conception to Tabakoff. Hedgewick, 497 F.2d at 908, 182 USPQ at 169; Mead v. McKirnan, 585 F.2d 504, 507, 199 USPQ 513, 515 (CCPA 1978). Since Nichols has not met its burden of proving the first prong of derivation, i.e., prior conception of the claimed subject matter, we do not reach the second prong of derivation, i.e., whether Nichols subsequently communicated its alleged conception to Tabakoff sufficiently to enable one of ordinary skill in the art to make and use the subject matter of the Count.

C. Conclusion

We hold that Nichols fails to prove an actual reduction to practice of the invention of the Count prior to Tabakoff's effective filing date of June 6, 1997. We also hold that Nichols has not proved derivation of the subject matter of the Count by Tabakoff.

IV. Deferred Nichols preliminary motion 1[14]

Pursuant to 37 CFR § 1.633(a), Nichols seeks judgment that involved Tabakoff claims 11-15, 18 and 19 are unpatentable under 35 U.S.C. § 102(f) for failure to name Nichols as joint inventors (Paper 33). Tabakoff opposes (Paper 45); Nichols replies (Paper 50).

In Fina Oil and Chemical Co. v. Ewen, 123 F.3d 1466, 1473, 43 USPQ2d 1935, 1941 (Fed. Cir. 1997), our appellate reviewing court said

> Conception is the touchstone to determining inventorship. See Sewall v. Walters, 21 F.3d 411, 415, 30 USPQ2d 1356, 1358 (Fed. Cir. 1994). Conception of a chemical substance requires knowledge of both the specific chemical structure of the compound and an operative method of making it. Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1921 (Fed. Cir. 1994).
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> * * * * * *
>
> ... [A] joint inventor must contribute in some significant manner to the conception of the invention. See Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1575, 37 USPQ2d 1626, 1632 (Fed. Cir. 1996) (citing Sewall, 21 F.3d at 415, 30 USPQ2d at 1358-59). As such, "each inventor must contribute to the joint arrival at a definite and permanent idea of the invention as it will be used in practice." Burroughs Wellcome, 40 F.3d at 1229, 32 USPQ2d at 1921.
>
> If a person supplies the required quantum of inventive contribution, that person does not lose his or her status as a joint inventor just because

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[14] In NICHOLS RESPONSE TO TABAKOFF PROPOSED FINDINGS OF FACT (p. 2, response to Tabakoff fact no. 16), Nichols confirmed that "Junior Party Nichols filed its Principal Brief on the issues of priority, derivation, and inequitable conduct (see Nichols Principal Brief)."

> If a person supplies the required quantum of inventive contribution, that person does not lose his or her status as a joint inventor just because he or she used the services, ideas, and aid of others in the process of perfecting the invention. See Shatterproof Glass Corp. v. Libbey-Owens Ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir. 1985).
>
> * * * * * *
>
> [However,], [t]he basic exercise of the normal skill expected of one skilled in the art, without an inventive act, also does not make one a joint inventor. See Sewall, 21 F.3d at 416, 30 USPQ2d at 1359.

Conception must include every feature or limitation of the claimed invention. Kridl v. McCormick, 105 F.3d 1446, 1449, 41 USPQ2d 1686, 1689 (Fed. Cir. 1997): Davis v. Reddy, 620 F.2d 885, 889, 205 USPQ 1065, 1069 (CCPA 1980). Inventor testimony alone is insufficient to prove conception; some form of corroboration must be shown. Price, 988 F.2d at 1194, 26 USPQ2d at 1036-37. Whether a putative inventor's testimony has been sufficiently corroborated is determined by a "rule of reason" analysis, in which "[a]n evaluation of all pertinent evidence must be made so that a sound determination of the credibility of the inventor's story may be reached. Id., 988 F.2d at 1195, 26 USPQ2d at 1037.

91. Here, there is no dispute that Tabakoff (Dr. Snell) contacted Nichols (Dr. Nichols) in December 1993 or January 1994 and asked Nichols to synthesize kynurenic acid derivatives wherein the 4-position of the kynurenic acid was substituted with a urea group in order to study their efficacy in treating alcohol withdrawal symptoms.[15]

92. Tabakoff admits that it did not suggest any method for making the requested compounds but denies that it did not suggest any particular type of urea group.[16]

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[15] See Paper 45, pp. 3-4 where Tabakoff partially admits Nichols fact 5 set forth in Paper 33, p. 3.

[16] See Paper 45, p. 4 where Tabakoff partially admits Nichols fact 8 set forth in Paper 33, p. 4.

93. Nichols' position is perhaps best summarized in its reply, i.e., "[t]he only significant fact is that conception and/or reduction to practice of the compound was not complete until Nichols conceived of the synthesis method, and therefore Nichols should have been included as a co-inventor on Tabakoff's application" (Paper 50, p. 6). (See also Paper 33, p. 8.[17])

94. In its opposition, Tabakoff primarily argues (a) Nichols preliminary motion 1 improperly raises issues of priority and derivation (Paper 45, p. 6) and, (b) even if Nichols independently devised a synthesis method, Tabakoff instructed Nichols as to what compounds to make and Nichols's method of making the involved compounds only amounted to the exercise of ordinary skill in the art (id., pp. 11-12).

A. The invention of Tabakoff claims 11-15, 18 and 19

As stated above, Tabakoff claim 12 is directed to a compound for treating withdrawal syndromes manifested in a patient suffering withdrawal symptoms and/or withdrawal-induced brain damage and having the formula (I):

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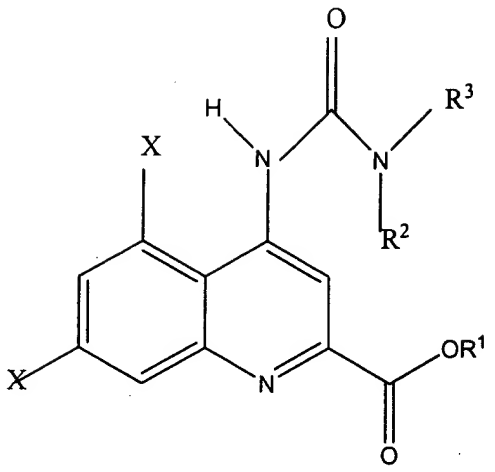
[17] In its motion, Nichols contends that

> ...First, conception of the invention was not even complete until Nichols conceived of the novel synthesis method, independent of any input from the Senior Party. ... Second, reduction to practice of the synthesis method and the organic compounds was conducted entirely by the Junior Party, with no contribution from the Senior Party. Third, Nichols' contributions to conception and reduction to practice were obviously significant, as Nichols' was responsible for all of the work with no assistance from the Senior Party. Finally, Nichols' work included the development of a novel synthesis method that was not found in any prior art, and therefore the Junior Party's work cannot be classified as merely using well-known concepts or current state of the art. [Paper 33, p. 8, citation omitted.]



a tautomer thereof, a pharmacologically acceptable ester, amide, salt, ether, or an acid addition salt thereof;

wherein R^1 represents hydrogen or an alkyl group of 1 to 3 carbon atoms;

R^2 and R^3 each independently represent phenyl which may be unsubstituted or alkoxy substituted one or more times with alkoxy containing 1 to 3 carbon atoms,

wherein each of the R^2 and R^3 substituents can be the same or different; and

X represents halogen and each of the 5, 7 substituents can be the same or different.

95. Tabakoff claim 13 specifies that each X is chloro, R^1 is hydrogen, and R^2 and R^3 are each phenyl. Tabakoff claim 14 specifies that each X is chloro, R^1 is a 1 to 3 carbon atom alkyl group, and R^2 and R^3 are each phenyl. Tabakoff claim 15 specifies that each X is chloro, R^1 is hydrogen, one of R^2 and R^3 is an unsubstituted phenyl and the other is a phenyl having a 1 to 3 carbon atom alkoxy substituent.

96. Tabakoff claim 11 limits the compound of claim 12 to (N,N-diphenyl)-4-ureido-

5,7-dichloro-2-carboxy-quinoline, (N,N-dipheny)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester or N-[2-methoxy]phenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline.

97. Tabakoff claims 18 and 19 are product-by-process claims wherein the products are (N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline methyl ester or (N,N-diphenyl)-4-ureido-5,7-dichloro-2-carboxy-quinoline, respectively.

98. Tabakoff's compounds are expressly "for treating withdrawal symptoms manifested in a patient suffering withdrawal symptoms and/or withdrawal induced brain damage" (Tabakoff claim 12).

99. Nichols relies on Exs 2012-2027 to support its motion.

100. As discussed above, Dr. Nichols testified that he conceived of a generic two-step process for making 4-urea kynurenates involving (1) attaching a carbonyl group to the 4-amino group of a 4-amino kynurenate and (2) attaching a secondary amine to the carbonyl group (Ex 2012, ¶ 38). Dr. Nichols further testified that used triphosgene (source of the carbonyl group) and various nitrogen-containing compounds to form 4-urea derivatives (id., ¶ 40). Among those various secondary amines were diethylamine and diphenylamine (see Exs 2021 and 2024).

101. In a letter from Dr. Nichols to Dr. Tabakoff, Dr. Nichols states, in part, that

> Dr. Yielding and I are please to have the opportunity to collaborate with you and Lohocla Research [Tabakoff's assignee] in the design and synthesis of compounds for the treatment of alcohol withdrawal. The series of compounds in which you have expressed an interest are 5,7-dichloro-4-ureido-2-carboxyquinolines. [Ex 2027, emphasis added.] [18]

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[18] Tabakoff's interest in this series of compounds is shown in several other letters of record. For example,

102. Dr. Nichols sent samples of several of his products to NIH for "anticonvulsant" testing and/or to Dr. Snell for "pharmacological" testing as discussed above (see e.g., Ex 2024, second page, and § III. Priority of this decision).

B. Analysis

It is Nichols burden to prove that it is a joint inventor of Tabakoff claims 11-15, 18 and 19 by a preponderance of the evidence. In re Caveney, 761 F.2d 671, 226 USPQ 1, 3 (Fed. Cir. 1985); 37 CFR § 1.637(a). In our opinion, Nichols fails to show that it "significantly" contributed to the invention of Tabakoff claims 11-15, 18 and 19 by a preponderance of the evidence.

1. claim interpretation

Initially, we note that "[i]f the body of the claim sets out the complete invention, and the preamble is not necessary to give 'life, meaning and vitality' to the claim, 'then the preamble is of no significance to claim construction because it cannot be said to

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(a) ...If, however, you [Dr. Yielding] and Al to proceed with a patent application prior to our getting data on the comparison of our compounds and those patented by Merck, I would like you both not to forget our conversation in Denver. The idea for generating the chemical structures (i.e., the ureido substituted kynurenates) originated with me, as did the postulate of the proposed biologic activity of, particularly, the diphenylureido derivatives. My postulates have been borne out by experiments in my laboratories. I, therefore, fully expect that any patent application on the ureido substituted kynurenates will have me definitely included as an inventor on the application. [Ex 2005, emphasis added.]

(b) ...I [Dr. Tabakoff] reiterate that the original idea to generate the dichloro,diphenylureidokynurenates belonged to me, and, as well, I proposed the physiological mechanisms by which such agents would express their anticonvulsant and other actions. ... [Ex 2006, emphasis added.]

(c) In terms of inventorship and other business-related issues, I would want the following: Given that the idea for the DCUKs [i.e., dichloro-diphenyl-ureido-kynurenates] originated with me [Dr. Tabakoff], ... (Ex 2007, p. 2, emphasis added).

constitute or explain a claim limitation.'" Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1373-74, 58 USPQ2d 1508, 1512 (Fed. Cir. 2001) (quoting Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed. Cir. 1999)).

103. During prosecution of the Tabakoff application, the examiner stated that "[c]ompounds having diphenylureido group have been used to inhibit the voltage sensitive sodium channels ... [and d]erivatives of kynurenic acid as antagonists of strychinine insensitive glycine binding at the NMDA receptor have been described." The examiner further stated that the "high degree of unpredictability in the NMDA receptor antagonist art and the voltage dependent sodium channel inhibitor art is well known. A slight change in the structure of the compound would drastically change its biological activity." Thus, according to the examiner, "generic claims ... [having] high affinity for both strychinine-insensitive glycine binding site on NMDA receptor and voltage dependent sodium channels ... [is] not commensurate in scope with the objective enablement, especially in view of the high degree of unpredictability...". [Office action mailed August 27, 1999 (Paper 4) in Tabakoff '697, pp. 3-4, ¶ 4, copy attached.]

Here, we conclude that the preamble of Tabakoff claim 12, i.e., a compound "for treating withdrawal syndromes manifested in a patient suffering withdrawal symptoms and/or withdrawal-induced brain damage," sets out a material claim limitation in that it provides a specific structural limitation requiring a kynurenic acid derivative that inhibits both voltage sensitive sodium channels and NMDA receptor function, specifically

strychinine-insensitive glycine binding.

2. Nichols fails to show that it "significantly" contributed to the invention of Tabakoff claims 11-15, 18 and 19

First, Nichols does not present any evidence that it knew of any **4-urea** kynurenic acid derivative prior to being asked to make 4-urea kynurenic acid derivatives by Dr. Snell, let alone the series of 5,7-dichloro-4-ureido-2-carboxyquinolines that Tabakoff expressed an interest in. Second, Nichols does not present evidence that it knew or appreciated that Tabakoff's claimed compounds required a structure that inhibited both voltage sensitive sodium channels and NMDA receptor function, specifically strychinine-insensitive glycine binding. Third, as discussed above (§ III. Priority), Nichols fails to establish that it would have required undue experimentation to synthesize Tabakoff's claimed compounds. Fourth, there is insufficient evidence to corroborate Nichols claim of joint inventorship, i.e., of a "significant" contribution, to the invention of Tabakoff claims 11-15, 18 and 19, with all of their claimed limitations.

In our opinion, Dr. Nichols performed routine synthetic activities on behalf of Tabakoff and sent samples of his work to NIH and/or Dr. Snell for testing, synthetic activities which Tabakoff has readily admitted. We take no position as to whether or not Nichols synthetic method is novel and unobvious. The process of making the involved compounds is not at issue in the sole count of the interference. As indicated in our earlier MEMORANDUM OPINION and ORDER (Paper 56, pp. 28-32), Nichols has not shown that Tabakoff method of making claims 16 and 17 are substantially identical to Nichols reissue application method of making claims 29-42.

For the above reasons, Nichols preliminary motion 1 is denied.[19]

V. Deferred Nichols preliminary motion 2

Pursuant to 37 CFR § 1.633(a), Nichols moves for judgment that Tabakoff compound claims 11-15, 18 and 19 are unpatentable due to inequitable conduct on the ground that Tabakoff intentionally withheld material information of inventorship with intent to deceive the PTO (Paper 34). Tabakoff opposes (Paper 46); Nichols replies (Paper 51).

A. Jurisdiction

Tabakoff argues that the Board has no subject matter jurisdiction on matters of inequitable conduct, "[i]n view of the recent decision in PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc., 225 F.3d 1315, 56 USPQ2d 1001 (Fed. Cir. 2000) ("... inequitable conduct is entirely equitable in nature... ") (Paper 46, p. 7).

First, there is nothing surprising in this statement as the very phrase "inequitable conduct" conveys an equitable nature. Second, the CAFC has long held that the issue of inequitable conduct is equitable, not legal, in nature. Kingsdown Medical Consultants, Ltd. v. Hollister Inc., 863 F.2d 867, 876, 9 USPQ2d 1384, 1392 (Fed. Cir. 1988) (en banc), cert. denied, 490 U.S. 1067 (1989). Third, according to the plain language of 37 CFR § 1.56(a) ("...no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct..."), the PTO can consider fraud and

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[19] The issue of whether Nichols compound claims 1-28 are unpatentable under 35 U.S.C. § 102(f) for failure to name party Tabakoff as joint inventors thereof is not before us and we decline to take up the matter sua sponte.

inequitable conduct issues. PTO policy, effective October 24, 1991, is that fraud and inequitable conduct issues will be considered when properly raised inter partes in patent interference cases. 1132 Off. Gaz. Pat. Off. 33 (November 19, 1991); GB v. CR, 23 USPQ2d 1158, 1159 (Bd. Pat. App. & Int. 1992).

A subsequent notice by the Chairman, Board of Patent Appeals and Interferences, explained the policy applied by the Board in determining whether the issues of fraud and/or inequitable conduct raised in a pending interference proceeding will be given consideration in 1133 Off. Gaz. Pat. & Tm. Office 22 (December 10, 1991). The notice explains

> Issue of fraud and/or inequitable conduct in an interference will be considered by the Board if:
>
> 1. They are raised by way of preliminary motion for judgement under 37 CFR 1.633(a). The motion must be filed during the period set for filing preliminary motions (37 CFR 1.636(a)), or good cause (37 CFR 1.655(b)(3)) must be shown as to why the issues of fraud and/or inequitable conduct were not timely raised during the preliminary motion period. An assertion that the issues were not raised earlier because the Board was precluded from considering them by the Commissioner's Notice of Oct. 17, 1988 (1906 Off. Gaz. Pat. Office 19 (Nov. 8, 1988)) shall not be deemed to be good cause.
> 2. They are raised by motion in a currently pending interference in which the time for filing preliminary motions expired prior to the publication date in the *Official Gazette* of the Commissioner's Notice dated Oct. 24, 1991, and *provided* (a) the motion is promptly after the *Official Gazette* publication date of the notice, and (b) the times for taking testimony or, if no testimony, the times for filing briefs for final hearing (37 CFR 1.656) have not been set.
>
> Issues of fraud and/or inequitable conduct will not be considered in any interference in which the times for taking testimony or the times for filing briefs for final hearing have already been set, unless "good cause" is shown under 37 CFR 1.655(b)(3). See item 1 above. An example of good cause would be where fraud or inequitable conduct is first discovered during taking of testimony.

> Interference parties are reminded that fraud and inequitable conduct must be established by clear, unequivocal and convincing evidence, and the party asserting misconduct carries a heavy burden of persuasion. *Driscoll v. Cebalo*, 731 F.2d 878, 221 USPQ 745 (Fed. Cir. 1984); *Norton v. Curtiss*, 433 F.2d 799, 167 USPQ 532 (CCPA 1970). Accordingly, unless evidence filed with a preliminary motion for judgement (37 CFR 1.639(a)) *prima facie* meets this standard of proof, the motion may be denied. If a party asserts that testimony is necessary to support or oppose the motion (37 CFR 1.639(c)), the requirements set forth in *Hanagan v. Kimura*, 16 USPQ2d 1791 (Comr. 1990), must be complied with; for example (16 USPQ2d at 1794):
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> > A proper request under § 1.639(c) must describe the nature of the testimony being sought. The description must be of sufficient detail so that the Examiner-in-Chief can determine whether or not there is a need for the requested testimony.
> >
> > * * * * * *
> >
> > If a person is to be called as a fact witness, a declaration by that person stating the facts should be filed new.
> >
> > If the other party is to be called, or if evidence in the possession of the other party is necessary, an explanation of the evidence sought, what it will show, and why it is needed must be supplied.
>
> Preliminary motions in the nature of "fishing expeditions," or based on broad assertions or argument of counsel, will not be permitted. Cf. *Price v. Folsom*, 208 USPQ 56 (Comr. 1980).

Neither Rule 56 nor the PTO advocate any change to Kingsdown.

Further, under 35 U.S.C. § 135(a), "[t]he Board of Patent Appeals and Interferences shall determine questions of priority of the inventions and may determine questions of patentability." Assuming arguendo that the inequitable conduct issue is not necessary to decide priority, a determination of inequitable conduct is committed to our discretion. Accord Critikon, Inc. v. Becton Dickinson Vascular Access, Inc., 120 F.3d 1253, 1255, 43 USPQ2d 1666, 1668 (Fed. Cir. 1997).

Therefore, the Board does have jurisdiction to consider issues of fraud and/or inequitable conduct raised in a pending interference if they are raised by way of preliminary motion for judgment under 37 CFR § 1.633(a) and filed during the period set for filing preliminary motions (37 CFR § 1.636(a)). Consequently, the Board has no jurisdiction to consider issues of fraud and/or inequitable conduct over claims not involved in the interference, i.e., any ruling hold such claims unpatentable for inequitable conduct would merely be an advisory opinion.

In order to convince us to exercise our discretion and hold that conduct amounts to "inequitable conduct," a party must show that its opponent (1) made an affirmative misrepresentation of fact or failed to disclose a fact; (2) the fact misrepresented or not disclosed was material; and (3) the misrepresentation or failure to disclose was done with intent to deceive or mislead the PTO. Molins PLC v. Textron, Inc., 48 F.3d 1172, 1178, 33 USPQ2d 1823, 1826 (Fed. Cir. 1995). "Materiality does not presume intent which is a separate and essential component of inequitable conduct" (id.).

The party alleging inequitable conduct on the part of its opponent bears a burden of proving its case by clear and convincing evidence. Manville Sales Corp. v. Paramount Sys., Inc., 917 F.2d 544, 552, 16 USPQ2d 1587, 1593 (Fed. Cir. 1990); Kingsdown, 863 F.2d at 872, 9 USPQ2d at 1389. Once the requisite levels of materiality and intent are shown, it is necessary to determine whether the equities warrant a conclusion that a party engaged in inequitable conduct. Molins PLC, 48 F.3d at 1178, 33 USPQ2d at 1827 (Fed. Cir. 1995).

In our opinion, there is no inequitable conduct because Nichols fails to prove by even a preponderance of the evidence, let alone by clear and convincing evidence, that Tabakoff believed Nichols to be joint inventor of its involved claims and withheld this information with intent to deceive the PTO. Thus, Nichols' inequitable conduct argument fails.

B. Nichols' inequitable conduct argument

Nichols contends that Tabakoff admitted Nichols (Drs. Nichols and Yielding) were co-inventors of Tabakoff's invention in a series of letters (Exs 2002-2007) from Dr. Tabakoff to Dr. Yielding which allegedly recognized the "significant" value of Nichols' contribution and offered to share patent revenues and ownership with Nichols. Nichols further contends that even if Tabakoff genuinely believed that Nichols were not joint inventors, Tabakoff's familiarity with the facts mandated disclosure to the PTO. [Paper 34, pp. 11-12; Paper 51, pp. 1 and 4-5.]

This last argument is somewhat surprising insofar as Nichols agrees with Tabakoff's opposition position, i.e., "Party Tabakoff correctly notes that a good faith disagreement over joint inventorship or an error in determining inventorship does not provide a basis for inequitable conduct" (NRB, p. 19).

C. Tabakoff's counter argument

Tabakoff argues that Nichols cannot be inventors of a compound they did not conceive and that the synthesis scheme allegedly used by Nichols to make the requested compounds was well within ordinary skill in the art. According to Tabakoff, a good faith disagreement over the law of joint inventorship vis-a-vis its compounds does

not provide a basis for inequitable conduct or give rise to a duty to raise an inventorship issue with the examiner, especially since Tabakoff does not claim Nichols' synthesis scheme. Finally, Tabakoff maintains that Nichols has failed to prove the requisite clear and convincing evidence of intent to deceive. [Paper 46, pp. 11-15.]

D. Analysis

"Inventorship" arises from conception, not development or reduction to practice, and is a question of who actually invented the claimed subject matter. Each inventor must contribute to the conception of the claimed subject matter, although each inventor need not make the same type or amount of contribution. It is undisputed that Nichols made 4-urea derivatives of kynurenic acid at the request of Tabakoff, i.e., that there was some type of collaborative relationship between Nichols and Tabakoff. However, collaboration per se does not itself produce joint invention any more than does the technical exchange of data pe se (or else NIH, Mr. Ezell, Dr. Seifert, etc., would also necessarily be co-inventors). Nichols fails to show that it "significantly" contributed to the invention of Tabakoff claims 11-15, 18 and 19 by a preponderance of the evidence as discussed in § IV. above.

1. the evidence does not show that Tabakoff believed Nichols to be joint inventors of the compounds of Tabakoff claims 11-15, 18 and 19

a. the Rule 63 declaration in Tabakoff '697 does not include Nichols

First, the Rule 63 declaration submitted in Tabakoff ' 697 only names Boris Tabakoff, Lawrence Snell and Paula L. Hoffman as inventors. Tabakoff, Snell and Hoffman each

> declare[d] that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that all statements made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon." [Rule 63 Declaration submitted with Paper 1 in application 09/171,697.]

b. Tabakoff did not move to correct inventorship

Second, Tabakoff has not filed a motion to correct inventorship of its application under 37 CFR § 1.634.

c. Tabakoff does not acknowledge Nichols as joint inventor in the letters proffered by Nichols (Exs 2002-2007)

Third, as discussed in more detail below, the series of letters proffered by Nichols (Exs 2002-2007) show that Tabakoff acknowledged Nichols' labor in synthesizing compounds and suggested that Nichols might have ownership rights in future patents. Ownership is separate from inventorship. Moreover, rather than acknowledging or suggesting that Tabakoff believed Nichols to be joint inventors of its claimed compounds, several of these proffered letters (Exs 2004-2007) are quite to the contrary.

i. the February 14, 1996 letter (Ex 2002)

104. A letter dated February 14, 1996 from Dr. Tabakoff to Dr. Yielding acknowledged that members of Dr. Yielding's laboratory synthesized twelve compounds as a result of early communications involving Dr. Snell [Tabakoff] (Ex 2002, ¶ 1). Dr. Tabakoff suggested that Lohocla Research Corporation [Tabakoff's assignee] and Dr. Yielding "come to a formal agreement on further research and pharmaceutical development of

the compounds you [Nichols] have already synthesized" (Ex 2002, ¶ 2). Dr. Tabakoff asked Dr. Yielding to consider:

> If compounds synthesized by you, or others in your company, prove through our research efforts to be efficacious in managing central nervous system hyperexcitability syndromes and have characteristics (i.e., bioavailability, appropriate therapeutic index, acceptable long-term toxicities, etc.) to be patented, you and/or your company and Lohocla Research Corporation would share, proportionately, in the patent. I would suggest that patents would be assigned, usually in a 50% / 50% ratio to your company and to Lohocla Research Corporation, respectively, ... unless one company or the other, committed a much more extensive amount of fiscal resources, time, and effort to the work necessary to patent the compound or to otherwise commercialize the compound. ... [Ex 2002, ¶ 3.]

105. In its principal brief, Nichols asserts that this letter (Ex 2002) shows that "Dr. Tabakoff clearly believed that the Junior Party had a claim of ownership to the twelve compounds that had already been synthesized and proposed that ownership of the patent would be based on the Junior Party's contribution of compounds and the Senior Party's contribution of methodology for managing central nervous system [CNS] hyperexcitability syndromes with the compounds" (NB, p. 48).

First, as stated in Sewall, 21 F.3d at 417, 30 USPQ2d at 1360,

> It is elementary that inventorship and ownership are separate issues. ... [I]nventorship is a question of who actually invented the subject matter claimed in a patent. Ownership, however, is a question of who owns legal title to the subject matter claimed in a patent, patents having the attributes of personal property.
> ...Who ultimately possesses ownership rights in that subject matter has no bearing whatsoever on the question of who actually invented that subject matter. [Citations omitted.] Beech Aircraft Corp. v. EDO Corp., 990 F.2d 1237, 1248, 26 USPQ2d 1572, 1582 (Fed. Cir. 1983).

Second, Tabakoff did not acknowledge that synthesis of the claimed compounds was not within ordinary skill in the art or that Nichols was the only one with an operable

method of making these compounds or assert that Tabakoff was a joint inventor of the synthesis method used by Nichols. Tabakoff simply acknowledged that Nichols made a number of compounds following its request, a fact not in dispute.

Third, patent rights might be assigned for any number of reasons, including as payment for services rendered. Tabakoff's suggestion to assign patent rights appears linked to a consideration of the "amount of fiscal resources, time, and effort" being expended would not be inconsistent such a reason. Such ownership rights have no bearing on the question of inventorship. Moreover, Tabakoff's proposal to include Nichols as a collaborator in a Phase II, SBIR application, which "application can include the testing of compounds you have synthesized ... [thereby providing monies] to establish the basic screening of the available compounds and for future synthesized compounds" (Ex 2002, ¶¶ 4-5), it not inconsistent with compensating Nichols for its past and future services rendered. Finally, reference to a "Phase II" application implies the prior existence of a Phase I application.

Therefore, the letter of February 14, 1996 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds.

ii. the February 28, 1996 letter (Ex 2003)

106. In the letter dated February 28, 1996, Dr. Tabakoff asked Dr. Yielding whether he thought that the compounds he and Dr. Yielding had been discussing might be covered under three recent, relatively broad-based patents enclosed with the letter (but not made of record). Dr. Tabakoff wanted Dr. Yielding's "critical assessment since the

further work on your compounds could certainly be influenced by these patents" (Ex 2003).

This acknowledges a fact not in dispute, i.e., that Nichols synthesized the compounds "we [Nichols and Tabakoff] have been discussing, and initially testing" (id.).

Therefore, the letter of February 28, 1996 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds.

iii. the letter of August 16, 1996 (Ex 2004)

107. In the letter dated August 16, 1996, Dr. Tabakoff expressed concern about a possible "divergent understanding" developing with Dr. Yielding, i.e.,

> Your [August 9th] letter contained some verbiage which generated in me [Dr. Tabakoff] the desire to follow up on the telephone conversation in which I discussed with you my origination of the idea to have synthesized the compounds which we are now studying. ... As mentioned in our earlier correspondence and conversation, I have no problem acknowledging the importance of Al's synthetic skills and I hope that agreements between us will give you and Al the proper credit and reward for your contributions. [Ex 2004, ¶ 1.]

108. Dr. Tabakoff also hoped that Drs. Yielding and Nichols could "be our guests in Denver so that we can review the Phase II application and discuss further activities with regard to the compounds already available and other collaborative possibilities discussed in our telephone conversations (e.g.: other Phase I applications originating from your laboratories)" (Ex 2004, ¶ 2).

Although this letter (Ex 2004) suggests tension is brewing between the parties, it does not contain any acknowledgment by Dr. Tabakoff that Nichols is a joint inventor of Tabakoff's compounds. Rather, Tabakoff clearly claims inventorship of the "compounds we are now studying." Tabakoff does not allege that it is a joint inventor of

the synthesis method used by Nichols to synthesize these compounds. Further, Dr. Tabakoff's hope to give Nichols "the proper credit and reward for ...[its] contributions" is not inconsistent with a hope to give Nichols compensation for services rendered.

Therefore, the letter of August 16, 1996 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds.

iv. the letter of January 17, 1997 (Ex 2005)

109. According to the letter from Dr. Tabakoff to Dr. Yielding dated January 17, 1997, "the review of our Phase II application" was attached thereto (Ex 2005, ¶ 1).

110. Dr. Tabakoff alluded to Nichols "anxiousness to submit a patent on the ureido substituted kynurenates" and wrote:

> If, however, you and Al wish to proceed with a patent application prior to our getting the data on the comparison of our compounds and those patented by Merck, I would like you both not to forget our conversation in Denver. The idea for generating the chemical structures (i.e., the ureido substituted kynurenates) originated with me, as did the postulate of the proposed biologic activity of, particularly, the diphenylureido derivatives. My postulates have been borne out by experiments in my laboratories. I, therefore, fully expect that any patent application on the ureido substitute kynurenates will have me definitely included as an inventor on the application. ... [Ex 2004, ¶ 2.]

Whatever Nichols might be planning to submit a patent application on, Dr. Tabakoff affirmatively claims inventorship of ureido substituted kynurenates, particularly, diphenylureido derivatives.

Therefore, the letter of January 17, 1997 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds.

v. the letter of March 17, 1997 (Ex 2006)

This letter suggests that a "major squabble" (Ex 2006, p. 2, last ¶) was developing between Tabakoff and Nichols.

111. Dr. Tabakoff wrote:

> I reiterate that the original idea to generate the dichloro,diphenylureidokynurenates belonged to me ... I do not argue the fact that you and Al Nichols, when asked, generated the synthetic scheme by which the kynurenate derivatives were synthesized .... [Ex 2006, p . 1, ¶ 1.]
>
> * * * * * *
>
> If you and Al wish to patent the chemical synthesis of the kynurenate derivatives, I certainly will not stand in your way... Given the information we have shared with you, it should be clear that not only the original idea, but its reduction to practice, has been pursued successfully in our laboratories. [Ex 2006, p. 1, ¶ 2.]

Again, the letter of March 17, 1997 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds or with Nichols inventorship of a possibly patentable method of synthesizing 4-urea kynurenates.

vi. the letter of April 17, 1997 (Ex 2007)

112. Dr. Tabakoff refers to "the route of synthesis for the DCUKs [dichloro-diphenyl-ureido-kynurenates] as developed by you [Dr. Yielding] and Al Nichols" (Ex 2007, p. 2, ¶ 1); a possible " 'prior art' [issue] with regard to patents already filed by Merck" (id., p. 2, ¶ 2), and states:

> In terms of inventorship and other business-related issues, I would want the following: Given that the idea for the DCUKs originated with me, and given that I directed the work in our laboratories on establishing the biological activity of these compounds, I would like my name to appear first on a list of inventors. This would be followed by the names of Al Nichols, Lawrence Snell, and you and Paula Hoffman. That patent would be assigned to Lochocla Research Corporation. Lohocla would enter into a contractual agreement with Yielding and Daugherty Research

> Enterprises, L.L.C. This agreement would state that any profits derived from the commercialization of the DCUKs would be divided in a way that Yielding and Daugherty Research Enterprises, L.L.C., receives 45% of these profits and Lohocla Research Corporation receives 55% of these profits. ... [Ex 2007, p. 2, ¶ 3.]

This letter suggests that Tabakoff believed a joint patent application with Nichols was possible, which application claimed DCUKs, their use as neuroprotective agents and a route of synthesis, and that any profits derived from commercialization of DCUKs would be shared between the respective companies of Tabakoff (Lohocla Research Corporation) and Nichols (Yielding and Daugherty Research Enterprises, L.L.C.). Consistent with the earlier letters discussed above, this letter suggests that Tabakoff believed itself to be inventor of the claimed compounds and their use as neuroprotective agents and believed Nichols to be inventor of a route of synthesis. This letter does not suggest that the synthesis of Tabakoff's claimed compounds required other than ordinary skill in the art or that methods of synthesis thereof other than that Nichols allegedly used to make these compounds at Tabakoff's behest did not exist.

Therefore, the letter of April 17, 1997 is not inconsistent with a good faith disagreement over joint inventorship of Tabakoff's claimed compounds.

In summary, the series of letters proffered by Nichols (Exs 2002-2207) are not inconsistent with an inference that Tabakoff had a good faith belief that it was the sole inventor of its claimed compounds; that Nichols may have a claim of ownership to the any profits due to the patenting of Tabakoff's claimed compounds since Nichols was responsible for making these compounds for Tabakoff; and, that Nichols may have invented a separately patentable method of synthesizing 4-urea kynurenates.

d. whether Nichols invented a separately patentable method for synthesizing 4-urea derivatives of kynurenic acids is not at issue in this interference

In its principal reply brief, Nichols argues that "it is still clear from these letters [i.e., Exs 2004-2007] that Dr. Tabakoff believed Party Nichols to be an inventor of at least the synthetic method for making the compounds" (NRB, pp. 19-20). Tabakoff has not alleged that it is an inventor of the method Nichols allegedly used to synthesize Tabakoff's claimed compounds. Indeed, in our prior MEMORANDUM OPINION and ORDER, we found that Nichols had not established that uninvolved Tabakoff method of synthesis claims 16-17 are the same patentable invention as uninvolved Nichols synthesis method reissue claims 29-42 (Paper 56, pp. 28-31).

Further, for the reasons discussed above in § III.B.1.b. Nichols fails to establish that synthesis of Tabakoff's claimed compounds would have required undue experimentation, i.e., was not within ordinary skill in the art. We take no position on whether the method Nichols allegedly used to synthesize Tabakoff's claimed compounds is itself patentable. Suffice to say the patentability of Nichols two-step synthesis method is not at issue in this interference.

e. summary

In summary, a good faith disagreement over the inventorship of Tabakoff's claimed compounds does not provide a basis for an inequitable conduct ruling. PerSeptive, 225 F.3d at 1321, 56 USPQ2d at 1005. Even an error in determining inventorship is not by itself inequitable conduct. Pro-Mold, 75 F.3d at 1576, 37 USPQ2d at 1632. Nichols has not proved that its synthesis method, which it performed

as a service to Tabakoff, constituted conception of the claimed compounds, i.e., that Tabakoff could not have synthesized the compounds without Nichols. The proffered evidence does not show the Tabakoff ever represented or acquiesced to inventorship of its claimed compounds by Nichols. Even if Tabakoff believed that Nichols had a claim of ownership to the compounds of Tabakoff claims 11-15, 18 and 19, ownership is a separate issue from inventorship.[20] Moreover, the letters discussed above suggest that Tabakoff made several offers to share ownership of any profits due to patenting of its claimed compounds with Nichols. A determination of inequitable conduct cannot be based on drawing inferences from inferences from inferences.

2. Tabakoff's "familiarity with the facts" did not mandate a disclosure to the PTO.

Nichols contends that Tabakoff had a duty to disclose "any information that establishes a prima facie case ... [Tabakoff] did not name the correct inventors in the [Tabakoff '697] application" (Paper 34, p. 9), even if Tabakoff genuinely believed that Nichols were not joint inventors (id., p. 11). According to Nichols, this information was that (1) Nichols independently conceived the allegedly novel method of synthesizing the compounds of this interference, (2) which led to the development of compounds having additional chemical groups attached to the urea substituent, all (3) without input from Tabakoff (id., pp. 9-10).

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[20] We note that in its principal brief Nichols argued that "[i]t is therefore a reasonable inference that the Senior Party did not disclose the Junior Party's claim of ownership to the USPTO to intentionally deceive the USPTO into issuing a patent to the Senior Party so that the Senior Party would have exclusive ownership of a potentially valuable pharmaceutical patent" (NB, pp. 25 and 50).

A good faith disagreement over that law of joint inventorship does not provide a basis for an inequitable conduct ruling. PerSeptive, 225 F.3d at 1320, 56 USPQ2d at 1004. Even an error in determining inventorship is not itself inequitable conduct. Pro-Mold, 75 F.3d at 1576, 37 USPQ2d at 1632. Moreover, an allegation of inequitable conduct is not established by a mere showing that art or information having some degree of materiality was not disclosed. FMC Corp. v. Manitowoc Co. Inc., 835 F.2d 1411, 1415, 5 USPQ2d 1112, 1115 (Fed. Cir. 1987). Further, a "failure to disclose" allegation of inequitable conduct may be rebutted by "a showing that applicant's failure to disclose art or information did not result from an intent to mislead the PTO" (id.).

3. the evidence does not show that Tabakoff acted with an intent to deceive the PTO

There is no dispute that Tabakoff asked Nichols to make 4-urea derivatives and that Tabakoff acknowledges that Nichols did so. We are not persuaded by Nichols' argument that the letters from Dr. Tabakoff to Dr. Yielding (Exs 2002-2007, discussed in § V.D.1.c. above) show by clear and convincing evidence that Tabakoff acted with an intent to deceive the PTO. Giving Nichols credit for work it performed at the behest of Tabakoff and offering to share ownership of future patent profits with Nichols is insufficient to establish by clear and convincing evidence that Tabakoff believed Nichols were joint inventors and intentionally hid this information from the PTO. It is just as plausible that Tabakoff merely wanted to compensate Nichols for work performed at Tabakoff's request. [Paper 34, p. 11.]

Nichols argues that deceptive intent can also be inferred from the letter of January 17, 1997 (Ex 2005), i.e., "[w]hen ... [Nichols] informed Tabakoff that they

intended to file a patent application directed towards the compounds, Tabakoff claimed that he should be included on the application, but never claimed Nichols and Yielding were not inventors" (Paper 34, p. 11). As discussed above (§ V.D.1. c.iv), whatever Nichols might have been planning to submit a patent application on, e.g., ureido substituted kynurenates, a method of synthesis thereof, a method of use therefore, etc., Tabakoff affirmatively claimed inventorship of at least the compounds. Rather, the letter of April 17, 1997 (Ex 2007) discussed above (§ V.D.1.c.vi.) suggested that Tabakoff believed a joint patent application with Nichols claiming ureido substituted kynurenates, a method of use and a method of synthesis thereof was possible. Nichols would have us infer that the Nichols' proposed application would claim only ureido substituted kynurenates and then make a second inference therefrom based on silence. A determination of inequitable conduct cannot be based on drawing inferences from inferences from inferences. Moreover, since we have concluded that Nichols is not a joint inventor of Tabakoff's claimed compounds, Dr. Nichols having synthesized these compounds was not material to any issue of patentability in this case.

Nichols would also have us infer deceptive intent on the part of Tabakoff because Tabakoff filed a patent application without naming Nichols as joint inventors after Nichols declined Tabakoff's "partnership offer" (Paper 34, p. 11; Paper 51, p. 7). Nichols further argues that Tabakoff may not have gotten its federal SBIR grant if NIH had known that Nichols "had a claim of ownership of the compounds claimed in the Tabakoff patent application" (id., p. 12). As stated above, ownership is a separate issue from inventorship.

Nichols points out that Tabakoff "published a technical journal article [Snell et al.[21]] relating to the compounds and their use, all without including the Junior Party. (Exh. 2008)" (Paper 34, p. 12). Nichols has not explained how Snell et al. (Ex 2008) shows that Tabakoff acknowledged Nichols as joint inventors, e.g., where Nichols' synthesis is described and/or stated to be the only operative synthesis. Snell et al. (Ex 2008) is not inconsistent with Tabakoff's position that Nichols is not a joint inventor.

4. it is Nichols' burden to establish inequitable conduct by clear and convincing evidence

Nichols faults Tabakoff for not offering "a single shred of factual evidence relating to the subjective intent of the inventors during prosecution of the patent" (Paper 51, pp. 7-8). In its principal reply brief, Nichols notes that its requested discovery to obtain evidence relative to the issue of inequitable conduct was denied (NRB, p. 20).

VI. The discussion in the ORDER DENYING NICHOLS MISCELLANEOUS MOTION 1 for discovery (Paper 41) is short and reads as follows:

> Nichols presents several reasons as to why "discovery" is needed.
>
> 1.
>
> Nichols seems to maintain that it has made out a prima facie case of inequitable conduct. Assuming, without deciding at this point, that inequitable conduct is an issue we can consider, and if so, that we should consider it, then if Nichols is correct, it will be successful. No further evidence should be necessary.
>
> However, the board suspects that Tabakoff will cross-examine at least Nichols. Tabakoff may also present evidence in support of its opposition, which may include declarations of relevant individuals named as inventors in the Tabakoff application. Nichols, of course, would be entitled to cross-examine.

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[21] Snell et al., "Novel Structure Having Antagonist Actions at Both the Glycine Site of the N-Methyl-D-Aspartate Receptor and Neuronal Voltage-Sensitive Sodium Channels: Biochemical, Electrophysiological, and Behavioral Characterization," The Journal of Pharmacology and Experimental Therapeutics, Vol. 292, No. 1, pp. 215-227 (2000) (Ex 2008).

> Given that Nichols believes it has presented a prima facie case, it is not apparent that Rule 639 discovery is necessary.
>
> 2.
>
> Nichols maintains that Tabakoff "could have a benign explanation for [allegedly] failing to inform the PTO" of certain information. If that be so, then one would fully expect Tabakoff in its opposition to Nichols Preliminary Motion 2 to offer up the "benign explanation."
>
> 3.
>
> The interference is in the preliminary motion phase. After the preliminary motion phase, there may be a priority testimony phase. Upon entry of a decision on preliminary motions, it also may be appropriate to defer to final hearing any issue of inequitable conduct and allow that issue to be developed along with priority.

Nichols now complains that Tabakoff did not present testimony refuting Nichols' allegations of inequitable conduct and argues that "the only reasonable inference is that Party Tabakoff did not have a good faith explanation and did not want to subject itself to cross-examination scrutiny" (NRB, p. 20). However, the initial burden is on Nichols to establish inequitable conduct on the part of Tabakoff by clear and convincing evidence. Only after Nichols satisfies its burden does the burden of persuasion shift to Tabakoff to rebut Nichols' allegation of inequitable conduct by "a showing that applicant's failure to disclose art or information did not result from an intent to mislead the PTO." FMC Corp., 835 F.2d at 1415, 5 USPQ2d at 1115. In our opinion, Nichols has not satisfied its initial burden by even a preponderance of the evidence, let alone by clear and convincing evidence.

For the above reasons, Nichols preliminary motion 2 is denied.

VI. Renewed Tabakoff preliminary motion 1

Tabakoff preliminary motion 1 was denied without prejudice, subject to renewal based on evidence acquired during the priority phase of this interference or other

evidence developed as a result of priority phase testimony (Paper 56, p. 42).

Tabakoff renewed its motion for judgment that Nichols claims 1-15 are unpatentable for failure to satisfy the best mode requirement of 35 U.S.C. § 112, first paragraph (TB, Paper 88). Nichols opposes (NO, Paper 96); Tabakoff replies (TRB, Paper 97).

As noted at final hearing, "if priority is not awarded to the junior party, then the best mode issue becomes moot" (Transcript, Paper 107, p. 32, ll. 18-19).

In view of our holding that judgment on priority as to Count 1 is awarded against junior party Nichols (see § III. above), renewed Tabakoff preliminary motion 1 is dismissed as moot.

VII. Order

It is

ORDERED that judgment on priority as to Count 1, the only count in this interference, is awarded against junior party, ALFRED C. NICHOLS and K. LEMONE YIELDING (**NICHOLS**);

FURTHER ORDERED that junior party, ALFRED C. NICHOLS and K. LEMONE YIELDING (**NICHOLS**), is not entitled to a patent containing claims 1-15 of U.S. Patent 5,783,700 or claims 1-28 of reissue application 09/625,018;

FURTHER ORDERED that, upon consideration of deferred Nichols preliminary motion 1 (Paper 33) and for the reasons given, Nichols preliminary motion 1 is **denied**;

FURTHER ORDERED that, upon consideration of deferred Nichols preliminary motion 2 (Paper 34) and for the reasons given, Nichols preliminary motion 2 is **denied**;

FURTHER ORDERED that in view of our judgment as to Count 1 awarding priority against junior party, ALFRED C. NICHOLS and K. LEMONE YIELDING (**NICHOLS**), renewed Tabakoff preliminary motion 1 is **dismissed** as moot;

FURTHER ORDERED that if there is a settlement agreement and it has not already been filed, attention is directed to 35 U.S.C. § 135(c) and 37 CFR § 1.661; and,

FURTHER ORDERED that a copy of this decision be given appropriate paper numbers and entered into the file records of U.S. Patent 5,783,700, reissue Application 09/625,018 and Application 09/171,697.

RICHARD E. SCHAFER
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

MICHAEL P. TIERNEY
Administrative Patent Judge

June 30, 2003
Arlington, VA

Enc: Office action mailed August 27, 1999 (Paper 4) in Tabakoff '697

104,522
cc (via overnight delivery):

Attorney for Nichols
(real party in interest
are the named inventors):

Kenneth M. Bush, Esq.
Russell L. Sandidge, Esq.
SIROTE & PERMUTT, P.C.
2311 Highland Ave. South
P.O. Box 55727
Birmingham, AL 35255-5727

Tel: 205-930-5100
Fax: 205-930-5101
E-mail: kbush@sirote.com
E-mail: rsandidge@sirote.com

Attorney for Tabakoff'
(real party in interest
Lahocla Research Corporation):

Talivaldis Cepuritis, Esq.
Dolores T. Kenney, Esq.
OLSON & HIERL
20 North Wacker Drive
36th Floor
Chicago, IL 60606

Tel: 312-580-1180
Fax: 312-580-1189
E-mail: olsonhierl@aol.com

INTERFERENCE DIGEST

Interference No. 104,522 Paper No. 9

Name: Boris Tabakoff et al.

Serial No.: 09/171,697 Patent No.

Title: COMPOUNDS, COMPOSITIONS AND METHOD SUITABLE FOR AMELIORATION OF WITHDRAWAL SYNDROMES AND WITHDRAWAL-INDUCED BRAIN DAMAGE

Filed: 10/23/98

Interference with Nichols et al.

DECISION ON MOTIONS

Administrative Patent Judge,_____ Dated,_____

FINAL DECISION

Board of Patent Appeals and Interferences, favorable Dated, 7-3-03

Court,_____ Dated,_____

REMARKS